Surgical Site Infection after Orthopedic Surgery Performed in Dong Guan Hospital of Traditional Chinese Medicine: A Descriptive Study of the Burden of Surgical Site Infection and its Risk factors with A Focus on Antimicrobial Prophylaxis and Traditional Chinese Medicine in Spinal Surgery

Jiancong Wang

Supervisor: Dr. Hanne Merete Eriksen

Co-supervisor: Prof. Gunnar Aksel Bjune

University of Oslo, Faculty of Medicine

Institute of Health and Society, Department of Community Medicine

Section for International Community Health

Thesis submitted as a part of the Master of Philosophy Degree

in International Community Health

11 May 2015

Contents

Acknowledgements

At first I would like to express my sincere appreciation to my supervisors, Dr. Hanne Merete Eriksen and Prof. Gunnar Aksel Bjune for their constructive guidance, supports and encouragements throughout my study and research process. They made me have such a great career in the two-year M.Phil research program in University of Oslo. Without them, this project would never have been possible.

I should thank to Prof. Magne Thoresen and Dr. Ibrahimu Mdala from University of Oslo to support on quantitative and statistical analysis on this project. Exclusive thanks should go to Prof. Akhtar Hussain and Prof. Johanne Sundby, and all the other professors who contributed to this master program. Thanks to all administrative staff at the department, especially Terese Eriksen who gave me a lot support and encouragement to overcome the challenges and difficulties during in my fieldwork and my study period. And a lot of thanks shall go to my classmate Dr. Socheat Cheng and my best friend Dr. Yuchuan Li in Norway for their genuine friendship.

I also wish to express my thanks to Dr. Xiaoyan Lu, the Dean of the Department of HAI-control; and Dr. Zhiwen Zheng, the President of the Dong Guan Hospital of Traditional Chinese Medicine for the greatest support of my study in Oslo and permit for this research. I sincerely express thanks to my colleagues Xinlei Ma, Kexin Qi, Weijuan Li, Fengmei Guo, who have given me great help and support during my study. I am also very grateful to Xiongfei Huang, Yongsheng Ye in the orthopedic ward, who took constant efforts to this project.

At last, special appreciation, of course, should go to my father Mr. Xiaohao Wang and my mother Ms. Anna Qi for great understanding, encouragement, and all the financial support to cover my two-year master study in Oslo.

Abstract

Surgical Site Infection after Orthopedic Surgery Performed in Dong Guan Hospital of Traditional Chinese Medicine: A Descriptive Study of the Burden of Surgical Site Infection and its Risk factors with A Focus on Antimicrobial Prophylaxis and Traditional Chinese Medicine in Spinal Surgery

Background: Surgical site infection (SSI) is a serious complication after orthopedic surgery, and it is associated with high morbidity rates, high healthcare costs and in some cases poor patients' outcomes.

Aims: The purpose of this study was to identify the burden of SSI among orthopedic surgery and its associated risk factors of SSI among the people underwent spinal surgery in a selected hospital in China.

Methods: From June 26 to November 30 in 2014, we performed a prospective surveillance study in the patients who underwent orthopedic surgery in a selected Chinese hospital. SSI was diagnosed based on the definition established by the Centers for Disease Control and Prevention (CDC) and was identified by bedside surveillance and post-discharge checkup. Detailed pre-, intra-, post-operative patient characteristics were prospectively recorded using a standardized data collection format.

Results: A total of 287 orthopedic surgery cases, among them 192 cases of spinal surgery, were included, of which 8 cases developed surgical site infection. Wound contamination class, wound drains and blood transfusion were surgery-related risk factors for orthopedic spinal surgery during the hospital stay after bivariate analysis. Intravenous AMP was given in 176 of 287 (61.3%) after orthopedic surgery. The average duration of AMP administration was 2.2 days (range 1-9 days).

Conclusion: In conclusion, we identified an incidence proportion of SSI after orthopedic surgery of 2.8%. The orthopedic SSI risk factors (wound contamination class, wound drains and blood transfusion) identified in present study may use to be reducing the incidence of SSI in the future.

Acronyms and abbreviations

HAI	Healthcare-Associated Infection
WHO	World Health Organization
SSI	Surgical Site Infection
CDC	Centers for Disease Control and Prevention
ECDC	European Centre for Disease Prevention and Control
THA	Total Hip Arthroplasty
PDS	Post-discharge Surveillance
ASA	American Society Anesthesiologists
AMP	Antimicrobial Prophylaxis
TCM	Traditional Chinese Medicine
GDP	Gross domestic product
CNY	Chinese Yuan
USD	US Dollar
BMI	Body Mass Index
95% CI	95% confident interval
OR	Odds ratio
SD	Standard Deviation

Surgical Site Infection after Orthopedic Surgery Performed in Dong Guan Hospital of Traditional Chinese Medicine: A Descriptive Study of the Burden of Surgical Site Infection and its Risk factors with A Focus on Antimicrobial Prophylaxis and Traditional Chinese Medicine in Spinal Surgery

1 Introduction

Healthcare-Associated Infections (HAIs) are infections that patients acquire while receiving medical care, and are one of the most frequent adverse events during care delivery [1]. HAI is a major problem for healthcare safety and can result in prolonged hospital staying, additional therapies, financial burdens, and even mortalities [2, 3]. Consequently, HAI control has been gradually receiving more public attention, with implementing effective practices such as surveillance to minimize the risk of infection and assure the patients' safety [4].

1.1 Burden of endemic healthcare-associated infections

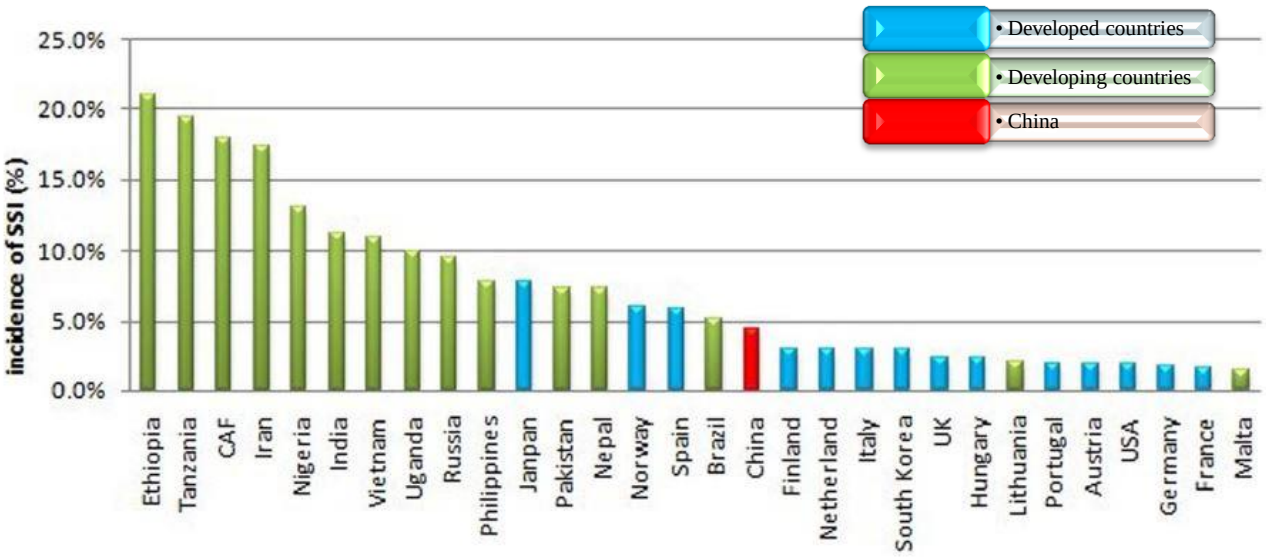
World Health Organization (WHO) report [5] from 2011 showed that the prevalence of HAI in low- and middle-income countries from 1995-2010 ranged from 5.7% to 19.1%[5], while this prevalence of HAI was significantly higher in high-income counties ranged from 3.6 to 12.0%. Stoesser et al.[6] showed that the overall HAI prevalence in a Cambodian study in 2013 was 13.8%. Kumar et al.[7] showed that the overall prevalence of HAIs in an Indian study in 2014 was 7%. Thu et al.[8] showed that the prevalence of HAIs in a Vietnamese study in 2011 was 7.8%. From review articles based on pre-studies [9-11] in China, it showed that the prevalence of HAI in all of China decreased from 5.2% in 2001 to 3.2% in 2012. A WHO report[5] discussed that the HAI surveillance in developing countries was a highly demanding task, and thereby only 23 of 147 developing countries reported a functioning national surveillance system of HAI.

Figure 1 Trends of the point prevalence of Healthcare-Associated Infections in China 2001-2012

1.2 Burden and consequences of surgical site infection

Surgical site infection (SSI) is a serious complication after orthopedic surgery, and it is associated with high morbidity rates, high healthcare costs and in some cases poor patients' outcomes[12]. SSI is reported to be the third most common HAI in Europe, U.S. and China [10, 13-15]

Figure 2 Incidence of surgical site infection in several countries around the world 2001-2012



A systematic review published in U.S. in 2013 by Korol et al.[16] showed that the median SSI incidence was 3.7%, ranging from 0.1% to 50.4%. An estimation based on European study in 2004[17] indicated that SSI can increase medical economic costs for hospital and health insurance companies, ranging from 1.5 to 19.1 billion Euro dollars per year.

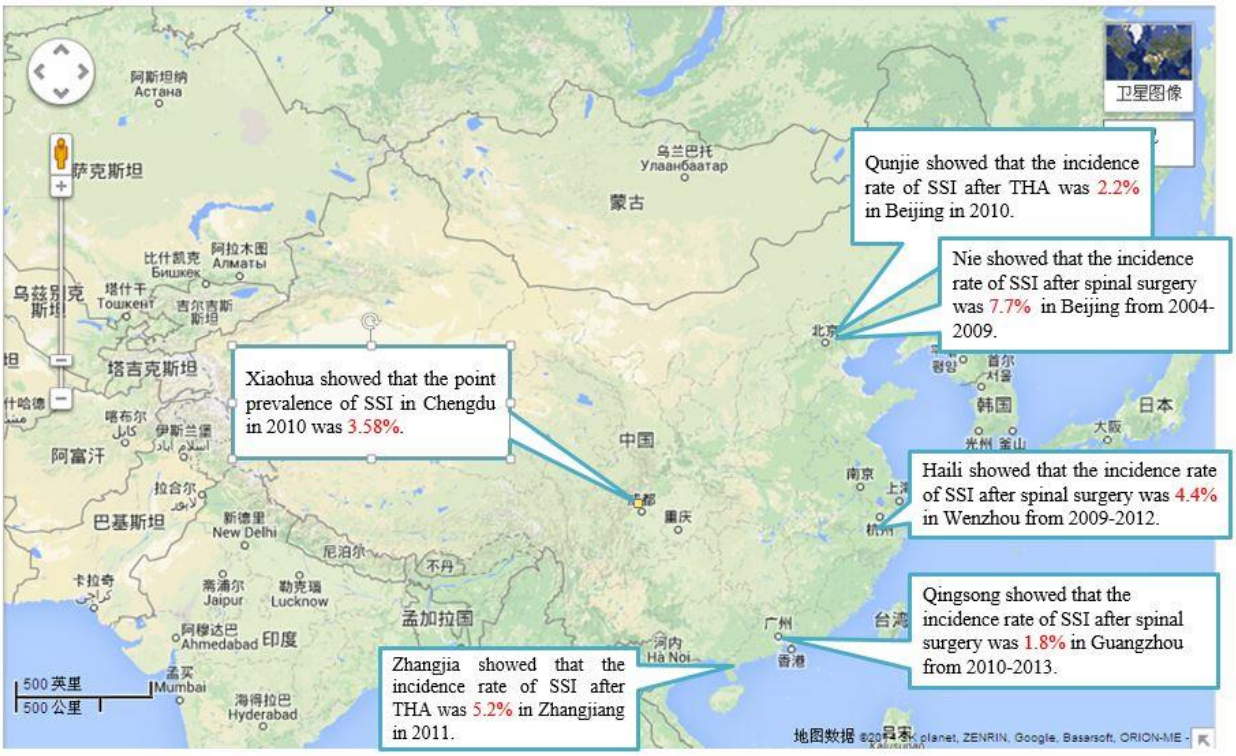
The magnitude of the burden of orthopedic SSI varies between different studies and different parts of the world by the type of orthopedic surgery performed. The overall incidence of orthopedic SSI reported from Monmouth Medical Center in U.S. between 2003 and 2007 [18] ranged from 0.8% for open reduction of fracture to 1.0% for a spinal fusion. From the European Centre for Disease Prevention and Control (ECDC) report 2008-2009[14], the cumulative incidence of SSI was 1.2% for hip prosthesis, and 0.8% for knee prosthesis, and 1.3% for laminectomy. Caputo et al.[19] showed that 3.7% of the orthopedic cases developed a SSI after spinal procedures at Duke University Medical Center in U.S. between 2005 and 2010. Mackenzie et al [20]showed the overall incident rate of SSI among pediatric patients undergoing spinal instrumentation to correct scoliosis was 5.8% in three children's hospitals in U.S. between 2006 and 2008. Kakimaru et al. [21] showed that the incidence of SSI among patients who underwent spinal surgery was 2.1% in Japan between 2003 and 2009. Lee et al [22] reported that patients with SSI have a higher rate of complication, and the SSI was a strong predictor of mortality (OR=3.8; 95% CI=1.5-9.7) after orthopedic surgeries.

Though retrieving on available literatures in China National Knowledge Infrastructure, it was identified that the incidence of SSI among patients with spinal surgery ranged from 1.8% to 7.7% across the country [23-25]. According the Guideline of Hospital Management and Assessment[26] published by Ministry of Health in China, the goal is that the overall incidence proportion of SSI after clean surgeries should be$\leqslant$1.5%. As seen below the published results are based on different type of orthopedic surgeries and are from different part of China.

Anhua et al.[9] showed in a national survey performed in China that the overall incidence of orthopedic SSI in 2012 was 2.8%. Qunjie et al.[27] showed that the incidence proportion of SSI after total hip arthroplasty (THA) was 2.2% in a selected hospital in Beijing in 2010. Zhangjia et al.

[28] showed that the incidence proportion of SSI after THA was 5.2% in Southern China in 2011. Nie et al. [23] showed in the study conducted at Capital Medical University in Beijing between 2004 and 2009 that 7.7% cases experienced postoperative infectious complication after spinal surgery. Haili et al. [24] found in the study conducted at Wenzhou Medical College between 2009 and 2012, an SSI proportion was 4.4% among patients undergoing spinal surgery. Qingsong et al. [25] showed in the retrospective study conducted at Southern Medical University China between 2010 and 2013 that the overall incident proportion of SSI among patients undergoing spinal surgery was 1.8%.

Figure 3 Incidence of surgical site infection based on different type of orthopedic surgeries and from different parts of China



1.3 Surgical site infection detected in post-hospital discharge surveillance

According to the Centers for Disease Control and Prevention (CDC) criteria SSI can occur up to 30 days (1 year if an implant is inserted) after surgery. The proportion of SSI identified after discharge varies by studies. Kent et al. [29] showed in the study conducted at St John of God Health Care

Australia between 1996 and 1998 that the rate of SSI in post-discharge surveillance (PDS) (6.0%) was more than double that in hospital (2.7%). Rosenthal et al.[30] showed in the study conducted at the University Hospital Basel Switzerland between 2000 and 2001 that the overall SSI rate was 4.7%, among from which 63.8% were detected in-hospital and 36.2% after discharge. Reilly et al. [31] showed in the Scottish Surveillance of Healthcare-Associated Infection Program between 2002 and 2004 that the SSI rate among the operations with no PDS was 2.61%, which was significantly lower than the SSI rate was 6.34% among the operations with PDS performed.

1.4 Risk factors of surgical site infection after spinal surgery

The incidence of SSI after spinal surgery could be influenced by patients' characteristics and pre-, intra- and post-operative factors. Following factors are shown to increase the risk of developing a spinal SSI: trauma, elder age, malnutrition, skin preparation not being performed, American Society of Anesthesiologists (ASA) score≥3, inappropriate timing of prophylactic antibiotic therapy, duration of surgical procedure≥3h, wound classified as contaminated or dirty, instrumentation, intraoperative blood loss, intraoperative blood transfusion, use of wound drains, and length of stays [13, 32-34]. However, a systematic review[32] indicated that there is a paucity of solid evidence of robust risk factors associated with spinal surgery.

1.5 Prophylactic antimicrobial of administration

Surgical Antimicrobial Prophylaxis (AMP) is designed for achieving effective antimicrobials concentration at the time of initial surgical incision, and maintained throughout the period of the procedures[35]. AMP administered properly is shown to reduce the incidence of SSI for patients[35]. The American Society of Health-System Pharmacists Therapeutic Guidelines[36] shows that AMP is not recommended for patients undergoing clean orthopedic procedures, including knee, hand, and food procedures, arthroscopy, and other procedures without instrumentation or implantation of foreign materials; while AMP is recommended for orthopedic spinal procedures with and without instrumentation. However, "Principle Guideline for Antimicrobials Clinical Use"[37] in China shows that AMP is not recommended in general, except

high risk factors, such as total hip arthroplasty, total knee arthroplasty, instrumentation and other factors. A review article[38] reported that the Ministry of Health in China issued a series of rules and regulations and guidelines. Most of them were general principles but not operational details. Through retrieving guidelines in Chinese database, there is no clear recommendation that AMP should be used for orthopedic spinal procedures in China.

In addition, according to "Principles and guidelines for clinical applications of prophylactic antibiotics" published by the Ministry of Health in China in 2004[39, 40], the general principle is that a single dose should be given in clean surgery less than 2 hour, and second dose should be given when surgery lasts more than 3 hour or blood loss exceeds 1,500 ml. The duration of prophylaxis should be less than 24 hours [38].

1.6 Microorganism of orthopedic surgeries

For most orthopedic SSI, the sources of pathogens are from the patients' own flora. Exogenous sources of SSI pathogens arise from surgical personnel, the operation-room environment, instrumentations and materials brought to the sterile field. Mackenzie et al [20] showed in a retrospective study from multicenter in U.S. from 2006-2008 that the three most common pathogens in spinal surgeries were *staphylococcus aureus, coagulase-negative staphylococci and Pseudomonas aeruginosa.* Antibiotic resistance has become more common and some studies [41, 42] have showed that methicillin-resistant *Staphylococcus aureus* (MRSA) is the most common organism in orthopedic SSI. A study [43] has shown that among 35 bacterial strains isolated after orthopedic surgery, 65.7% were gram-positive isolates, and 34.3% were gram-negative bacteria; 68.6% of all bacterial isolates were resistant to cefuroxime after orthopedic surgery.

2 Rationale of the study

A surveillance system is a method for understanding the incidence and distribution of SSI [44]. In China, public reports of SSI, obtained via ongoing national surveillance activities, have been rare over the past decades [45]. The computerized search strategy resulted in 33 citations in the last five

years by the key words “Spinal”, “Surgical site infection” and “China” into the PubMed (English) search engine. This indicates a paucity of quantitative research regarding the burden and associated risk factors of SSI among the people with orthopedic surgeries in Dong Guan community as well as in China. Most of the articles from China published in PubMed were description of clinical therapy and clinical trial research on orthopedic surgery, and not included SSI. The focus on orthopedic SSI in Dong Guan community has just started and the resources for orthopedic SSI-control have been insufficient. Given this situation, the president of the hospital and the dean of the department of HAI-control wanted and had permitted this collaboration research. The goal of this study was to fill the knowledge gaps of HAI-control in this hospital, and it could contribute to the reduction of the occurrence of SSI.

Another rationale for this study was that the search in PubMed showed no literatures of quantitative study discussing the use of traditional Chinese medicine (TCM). The only findings about TCM (such as *Panax notoginseng saponins*)[46] showed that they not only have immunomodulatory and antimicrobial effects, but also have biological effects on anti-inflammatory, promoting circulation and supporting tissue/bone healing[47, 48]. This project aims to fill this knowledge gap, by discussing the use of TCM.

The literatures [32] on SSI following spinal surgery shows that a total of 73 different types of factors were evaluated as risk factors of SSI but it was still stated a need for more researches[32]. This project was built upon the existing surveillance system, but it also included additional variables referred by CDC and studied articles [23, 49-53]. A goal of this project was to examine the effect of different types of risk factors of orthopedic SSI following spinal surgery emerging during the pre-, intra- and post-operation in the hospital setting, in order to target specific risk factors.

3 Objectives and research questions

Overall objective

To identify the burden of SSI in orthopedic surgery and its associated risk factors among the people

undergoing spinal surgery in Dong Guan Hospital of Traditional Chinese Medicine in China between June 26 and November 30 in 2014.

Specific aims

• To identify the total incidence proportion of SSI at the time of hospital discharge as well as 30 days post-surgery.

• To identify the total incidence proportion of SSI by type of orthopedic surgery.

• To identify the most common micro-organisms associated with orthopedic SSIs as well as their antimicrobial susceptibility patterns.

• To identify possible risk factors of SSI after spinal surgery

•To explore the use and possible associations of AMP and TCM on the rate of SSI.

4 Materials and methods

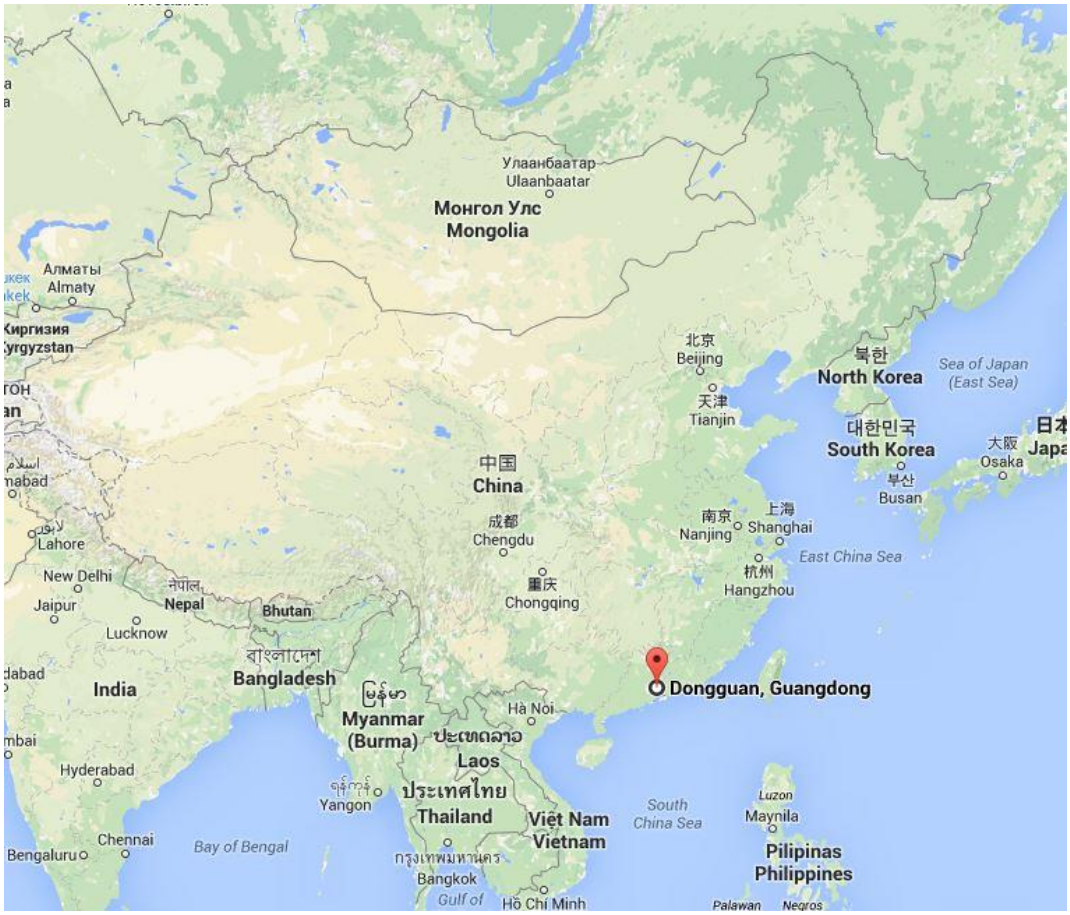
4.1 Brief description of the study site

Dong Guan City is located in the southern China and adjoined to Hong Kong. It is a relatively developed region with abundant healthcare resources in China, with a total Gross Domestic Product(GDP) of 473.5 billion CNY (approximately 76 billion USD) in 2011 and its GDP per capita of 9,190 USD[54] (compared with 100,818 USD GDP per capita in Norway in 2013 [55]). The publications from the Health Bureau of Dong Guan City [56] showed that by 2010 the average life expectancy of the city will exceed 77 years. The infant mortality rate is below 10 deaths/1,000 live births (<11deaths/1,000 live births in China).

In 2005, the total expenditure on health service reached 285.9 million CNY (45.8 million USD), accounting for 2.0% of the financial budget [56]. It was estimated that in 2010 in Dong Guan City the ratio of doctors to nurses was1:1.2. The ratio of available beds against clinical doctors was 1:0.4 with the ration for ICU reaching 1:2.5-3. The number of practicing (assistant) doctors, registered nurses and hospital beds by thousand people was 1.7, 2.0 and 3.1 respectively.

The Health Bureau of Dong Guan City recommended healthcare providers and healthcare-settings to undertake tasks of HAI-control and surveillance, improve outbreak surveillance system and pre-warning system, and strengthen the construction of professional teams which are focusing on upgrading the capability of investigation about epidemic diseases[56].

Figure 4 Geographical location of Dong Guan City in China



4.2 Dong Guan Hospital of Traditional Chinese Medicine and its surveillance and infectious control program

The Dong Guan Hospital of Traditional Chinese Medicine is a tertiary hospital, with an integrated function of medical treatment, teaching and research, with 955 hospital-beds. According to "Nosocomial Infectious Control Measurement"[57] published by the Central People's Government of the People's Republic of China in 2006, a Hospital Infectious Control Committee has been established. Its responsibility is HAI-control training and meeting with infectious control

practitioners, infectious information feedbacks, and identification and management of HAI-outbreak. According to “Standard for nosocomial infection surveillance WS/T312-2009” [58] published by the Health Industry Standard of the People's Republic of China in 2009, the Dong Guan Hospital of Traditional Chinese Medicine has established a prospective surveillance system of orthopedic SSI[59].

4.3 Traditional Chinese Medicine used in Dong Guan Hospital of Traditional Chinese Medicine

Development of TCM is based on the concept of *Yin and Yang*. These opposing and complementary natural phenomena of the universe restore the normal physiological functions, consequently curing diseases and restoring health of a patient[60]. Surgeons and physicians in the Dong Guan Hospital of Traditional Chinese Medicine usually use an integrated clinical treatment/integrative practice. According to the clinical condition of the patients, surgeons with TCM background choose selected herbs as supplementary treatment to enhance the efficacy of western medicine, with inhibiting effect on the inflammatory responses, promoting blood circulation, and removing the swelling [46, 61, 62]. According to property of TCM, patients are treated with TCM in a highly individualistic way, recognizing that not two patients are alike. However, the therapy is not strictly evidence-based because of lacking enough clinical studies [63].

4.4 Rationale for the choice of research method

The systematic review showed that different methodologies[64] were used in orthopedic SSI surveillance. It is recommended to use prospective cohort study to detect orthopedic SSI[65]. The advantage of this study-method is that it provides the reliable and less biased datasets by applying daily observation, and it allows you to identify possible associated risk factors for orthopedic SSI. Potential disadvantage is that prospective surveillance is more time-consuming and that a large sample size is required to identify associated risk factors. However, the case-control design and cross-sectional method is not recommended in the orthopedic SSI surveillance system, due to the limitations that they cannot be used to the incidence proportion of orthopedic SSI[65].

Cross-sectional study is not suitable to use to identify associated risk factors[65].

4.5 Research design

The study was conducted as a prospective cohort study focusing on patients undergoing orthopedic surgery in the Dong Guan Hospital of Traditional Chinese Medicine, affiliated to Guangzhou University of Chinese Medicine between June 26 and November 30 in 2014.

4.6 Study population

The study included all patients in the Dong Guan Hospital of Traditional Chinese Medicine who undergoing orthopedic surgeries at an orthopedic surgery ward between June 26 and November 30 in 2014. No patients were excluded from this study.

4.7 Sample size calculation

In the study, we would have been conducted as a prospective cohort study focusing on all the patients undergoing orthopedic surgery at an orthopedic ward in the hospital. The initial design used an estimate of the incidence of orthopedic SSI[66] approximately ranged from 1.8% to 7.7% according to literature review. In order to detect an orthopedic SSI, with an assumed odds ratio of 5.8 and a prevalence of 2%, we need a sample of 244 cases to achieve a power of 80%.

4.8 Definition of surgical site infection

All SSI-cases are defined according to the CDC-criteria for SSI diagnosis (Annex 1)[67], and SSI are classified as incisional or organ/space. Incisional SSIs are divided further into superficial incisional SSI or Deep superficial SSI [65, 67].

4.9 The preparation of the study

The surveillance was conducted by personnel in the Department of HAI-control and personnel in an orthopedic ward. Even though this project was in accordance with the ongoing surveillance system,

the investigator (the author of this thesis) developed a protocol (See Research Protocol) and specific questionnaire including more potential risk factors and PDS (Annex 9 and 10). The permission to conduct the study was needed and given by both the dean of the department of orthopedics and the president of the hospital.

4.10 Sources of information

The sources of information in this study was from hospital records, medical records, medical progress notes records, procedure-related records, anesthesia record sheets and surgical risk assessment form. These datasets were captured from Hospital Informatics Systems.

Figure 5 Hospital Informatics Systems in the Dong Guan Hospital of Traditional Chinese Medicine

4.11 Surgical site infection registration

If a patient who had two operations more than thirty days apart each operation was recorded independently of each other. If the second operation was a result of SSI it was recorded as a consequence of the SSI. If re-operated for reasons other than SSI, the total number of operations within thirty days was recorded as a potential risk factor. The patient was followed up thirty days after the first operation.

4.12 Data collection and case finding

In the hospital, identification of potential SSI was done by the examination of the patient medical records, microbiology reports, nursing notes, International Classification of Diseases, Ninth Revision codes, and antimicrobials used. The investigator performed actively bed-side observation three days a week (Monday, Wednesday and Friday). The wounds of those patients that had prescribed antimicrobials, had a temperature over 37 Degree Celsius or relevant co-morbidity that easily caused SSI was examined.

Surgeons daily visited the patients with orthopedic surgeries, reviewed their medical records and supervised the wounds. The questionnaires (Annex 9) were filled by surgeons and thereafter reported to the department of HAI-control, if a SSI was identified. In addition, clinical pharmacists reported actively the suspected-SSI with irrational antimicrobials prescription to surgeons and investigator.

During the hospital stay, some patients with co-morbidities such as heart diseases, diabetes mellitus could be transferred to other wards for further medical treatment. The main investigator continued to follow these patients until 30 days after surgery and filled in questionnaire (Annex 9) before discharge.

4.13 Post-discharge surveillance and case finding

Phone call

According to the CDC-criteria, the SSIs might occur up to 30 days post-surgery. The investigator would follow up the patients via telephone interview using a pre-defined script of questionnaire for the detection of SSI. During the interview the investigator asked the patients with questions (Annex 10) and the answers only documented by “YES” or ”NO” to evaluate the wound status of patients. Before the interview, oral informed consent would be obtained.

Post-discharge examination checkup

All the patients received an appointment for a post-discharge examination at the out-patient clinic

but it was not mandatory. The investigator also participated on the out-patients clinical round during changing the wound dressings, with examination of the incisional sites for pain, redness, warmth, swelling and purulent drainage. However, it was found to be difficult for the investigator to follow up those patients who did not attend the post-discharge checkup.

Readmission

The surgeons would have been asked by investigator to actively report the post-discharge infections being detected at outpatient clinic, if the patients readmitted for surgery were surveyed for infections.

4.14 Microorganism

For the bacteria isolation, specimens were inoculated onto blood agar plates, incubated in an aerobic chamber at 37°C, and examined at 48 and 96 hours. Laboratory technicians trained the surgeons in how to acquire the appropriate sample from the surgical site, and stress the use of asepsis technique. Laboratory technicians informed the surgeons and the investigator of confirmation of positive microorganism, even Multidrug-Resistant Organisms [68].

4.15 Included variables and data handling

This project included all variables (Annex 6) which were already in the hospital surveillance system such as age, gender, ASA scores, wound contamination class, duration of surgical procedures, type and duration of AMP administrated; as well as risk factors referred by CDC and identified by studied articles [23, 49-53], such as BMI, diabetes mellitus, rheumatoid arthritis, bone oncology, type of anesthesia, pre-operative stay, instrumentations, skin-preparation, number of participants attending to the orthopedic surgeries, intraoperative blood loss, wound drains, duration of wound drainage, intraoperative blood transfusion, TCM administrated, white blood cell count before/after surgery, bacteria isolation and length of stays.

All data was electronically recorded and thereafter transferred to the department of HAI-control.

The investigator translated information into English, and then filled out the study data-form. All data was entered into a Microsoft *Excel2010* file.

4.16 Data validation

The investigator and his colleagues in the department of HAI-control were responsibility for the data validation. All the questionnaires (Annex 9) were validated against information recorded in the patient's medical file to assure that all the correct data was being filled in. If some datasets were incorrect or missing information, the surgeons would be asked to fill in and correct them. A SSI case was confirmed and ensured the agreement between the surgeons and investigator. If diagnosis of a SSI-case was disagreed by both, the investigator would judge and diagnose a SSI-case according to CDC-criteria (Annex 1).

4.17 Training

All the staffs included in this surveillance were trained by the investigator one week before the project started. Training included information about the data collection methods as well as the principle of diagnosis of SSIs according to CDC-criteria (Annex 1). A key emphasis was that all the needed information in the questionnaire (Annex 9) should be filled in, and it should be assured that the datasets were authentic and correct. This surveillance system of SSI has been conducted since 2008 in this hospital. We therefore regarded it as unnecessary to perform a pilot-testing to test and refine the survey methods.

5 Statistical analysis

The datasets were analyzed using IBM SPSS Statistics Software Version 22.0. Descriptive statistical analysis was run. Mean, 95% confidence interval (Cl), minimum and maximum of each continuous variable was calculated.

Only spinal procedures were included in risk factors analysis knowing that this was the most

common procedures in this study. Patient's characteristics related to SSI were compared by using *Chi-square* test or *Fisher's exact* test for categorical variables and the by using *Wilcoxon* test for continuous variables. Associations between SSI and possible risk factor were analyzed by calculating crude Odd's Ratio (OR) using Bivariate Logistic Regression Analysis.

6 Ethical considerations

Ethical clearance was obtained both from "Regionale Komiteer for Medisinsk og Helsefaglig Forskningsetikk" from Norway and Ethics Committee from the Dong Guan Hospital of Traditional Chinese Medicine (Annex 11,12 and 13). The questionnaires (Annex 9 and 10) were locked and kept securely by the project leader. Participants were anonymous in the questionnaire. Only the investigator and his colleagues had an access to review and manage these datasets.

This study was regard as a quality assurance project and was therefore unnecessary to obtain informed consent from the each patient. Only information already documented in patient file was included in this project, with the exception of the 30 days following up by phone.

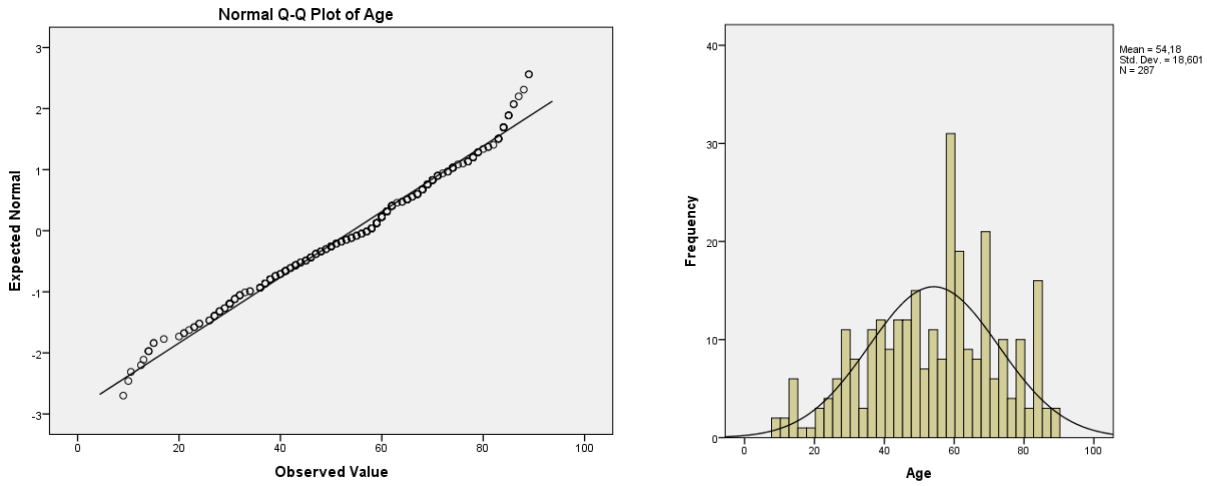
Our project did not provide intervention and did not include any harm for the patients. When contacting patients by phone after hospital discharge, we informed them about the project and they could choose not to answer to questions regarding SSI-study.

7 Results

7.1 General description and demographical data

All 287 patients that had orthopedic surgeries between 26 June and 30 November in 2014 were included in the study. There were 165 females (57.5%) and 122 males (42.5%). The mean age was 54.2 years (range, 9-89 years), and it was higher among women than men (60.7 years VS 45.4 years). The age as continuous variable followed a normal distribution (Figure 6).

Figure 6 Normal distribution in Age



The mean days of pre-operative stay was 6.6 days (range, 1-33 days). The mean total days of hospital stay was 16.8 days (range, 4-77). The mean duration of surgery was 116.3 minutes (range, 20-575). More demographical characteristics are found in Table 1.

Among the 287 orthopedic surgeries, 67 (23.3%) patients had hypertension, 23 (8.0%) patients had diabetes mellitus, 11 (3.8%) patients had rheumatoid arthritis, 23 (8.0%) patients had bone oncology, 114 (39.7%) patients had wound drainage, and 28 (9.8%) patients had intraoperative blood transfusion.

The most common procedures performed in this orthopedic ward were spinal surgery with 192 cases (66.9%), followed by clavicular surgery (5.2%), tibia surgery (5.2%), and anklebone surgery (4.2%). According to categorization of ICD-9-CM codes, the three most common spinal surgery procedures in the present study were vertebroplasty (51.0%), spinal decompression (14.6%), and spinal fusions (7.3%).

7.2 Surgical site infection detected during in-hospital and post-discharge

Among the 287 orthopedic surgeries, 8 (2.8%) patients developed SSI. All SSIs were detected

among in-hospital patients and no SSI was detected by PDS. According to the CDC definition, 4 (1.4%) of infections were superficial incisional SSI, 4 (1.4%) of infections were deep Incisional SSI and no case was diagnosed with Organ/Space SSI (Table 1). In addition, among the 192 orthopedic spinal surgeries, 7 (3.6%) patients developed SSI after spinal surgery, with 3 (1.6%) patients of superficial incisional SSI and 4 (2.1%) patients of deep incisional SSI.

7.3 Risk factors for spinal surgery

Bivariate analysis indicated several significant risk factors, including wound contamination class (OR, 45.5; 95% Cl, 6.9-298.8), wound drains (OR, 8.8; 95% Cl, 1.0-74.6), blood transfusion (OR, 5.6; 95% Cl, 1.2-26.5) (Table 4).

7.4 Routines of antimicrobial prophylaxis and traditional Chinese medicine

Intravenous AMP was given in 176 of the 287 (61.3%) after orthopedic surgeries. In addition, 34 other cases received antimicrobials treatment at the time of surgery. 174 of 176 (98.9%) received AMP within 2 hours before the orthopedic procedures. The average duration of AMP administrated was 2.2 days (range 1-9 days) (Table 2). In addition, intravenous AMP was given in 120 of the 192 (62.5%) after orthopedic spinal surgeries.

The four most common AMP prescribed were cefotiam (35.8%), cefathiamidine (22.2%), cefuroxime (17.6%) and cefamandole (9.1%) (Table 2). These four prescriptions contributed to 84.7% of the total AMP given. All the 8 patients who developed SSI did receive AMP.

TCM was prescribed to 219 of the 287 patients (76.3%). The three most common TCM deliveries in the present study were *Panax notoginseng saponins* (55.7%), *Salvia miltiorrhiza* (23.7%), and *Lumbricus rubellus* (11.9%) (Table 3). More specific functions of common TCM are found in Annex 8.

7.5 Microorganism

Among the 8 patients developed SSI, only 4 patients had performed wound bacterial culture. 2 of 4 SSIs were examined and identified microorganisms, among one case being documented as Multi-Drug Resistant Organism [E.coli + Extended-Spectrum Beta-Lactamases (ESBLs)] (Table 6). It was resisted towards 69.6% of the available antimicrobials in this hospital.

Table 1 General description and demographical information for patients undergoing orthopedic surgery at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014

Patient's characteristics	All orthopedic surgery
The total number of procedures (cases)	287
Male (%)	122 (42.5%)
Female (%)	165 (57.5%)
Mean age in years (range)	54.2 (9-89)
Mean days of pre-operative stay (range)	6.6 (1-33)
Mean total days of hospital stay (range)	16.8 (4-77)
Mean duration of surgery in minutes (range)	116.3 (20-575)
The number of SSI [a] (%)	8 (2.8%) [b]
The number of Superficial SSI [a] (%)	4 (1.4%) [c]
The number of Deep SSI [a] (%)	4 (1.4%) [d]
The number of SSI [a] diagnosed in-hospital (%)	8 (2.8%)

[a] *SSI: Surgical Site Infection*

[b] *7 of them were after orthopedic spinal surgery*

[c] *3 of them were after orthopedic spinal surgery*

[d] *All of them were after orthopedic spinal surgery*

Table 2 Descriptive analysis of AMP among all the orthopedic surgery at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014 (N=287)

Patient's characters	All orthopedic surgery
AMP administrated (%)	176 (61.3%)
AMT administrated (%)	34 (11.8%)
AMP deliveries given within 2 hours before the orthopedic surgery (%)	174 (98.9%)
Mean of duration of AMP deliveries in day (range)	2.2 (1-9)
The type of AMP (%)	-
cefotiam	63 (35.8%)
cefathiamidine	39 (22.2%)
cefuroxime	31 (17.6%)
cefamandole	16 (9.1%)
cefoxitin	9 (5.1%)

**AMP: antimicrobials prophylaxis; AMT: antimicrobials treatment*

Table 3 Descriptive analysis of TCM among all the orthopedic surgery at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014 (N=287)

The type of constituents of TCM	All orthopedic surgery
TCM deliveries (%)	219 (76.3%)
Panax notoginseng saponins	122 (55.7%)
Salvia miltiorrhiza	52 (23.7%)
Lumbricus rubellus	26 (11.9%)

**TCM: traditional Chinese medicine*

Table 4 Risk factors of SSI among patients undergoing spinal surgery at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014 (N=192)

Patients characteristics (Variables)		Total number patients of operations (SSI case)	Odds ratio (95% Cl) Bivariate analysis
Age	Age≤62yrs	105 (5)	Reference Cat.
	Age>62yrs	87 (2)	0.5 (0.1-2.5)
Gender	Female	130 (5)	Reference Cat.
	Male	62 (2)	0.8 (0.2-4.4)
Body Mass Index (BMI)	BMI≤25	119 (6)	Reference Cat.
	BMI>25	15 (1)	1.3 (0.2-12.0)
	Missing	58 (0)	-
Rheumatoid arthritis	Yes	7 (1)	5.0 (0.5-48.0)
	No	185 (6)	Reference Cat.
Pre-operative stay	≤7 Days	140 (5)	Reference Cat.
	>7 Days	52 (2)	1.1 (0.2-5.7)
Orthopedic instrumentation	Yes	60 (4)	3.1 (0.7-14.2)
	No	132 (3)	Reference Cat.
American Society of Anesthesiologists (ASA) scores	1+2	165 (5)	Reference Cat.
	3	27 (2)	2.6 (0.5-13.9)
Wound contamination class	Class 1+2	186 (4)	Reference Cat.
	Class 3+4	6 (3)	45.5 (6.9-298.8)
Skin preparation	Yes	167 (6)	Reference Cat.
	No	25 (1)	1.1 (0.1-9.7)
The duration of operation	<3h	146 (5)	Reference Cat.
	≥3h	46 (2)	1.3 (0.2-6.8)
The number of participants in the orthopedic surgery	3-5 participants	122 (2)	Reference Cat.
	6-9 participants	70 (5)	4.6 (0.9-24.5)
Intraoperative	<500ml	162 (4)	Reference Cat.

blood loss	>500ml	30 (3)	4.4 (0.9-20.7)
Wound drains	Yes	81 (6)	8.8 (1.0-74.6)
	No	111 (1)	Reference Cat.
Blood transfusion	Yes	25 (3)	5.6 (1.2-26.5)
	No	167 (4)	Reference Cat.
WBC before surgery	4-11×10^9/L	158 (5)	Reference Cat.
	>11×10^9/L	34 (2)	1.9 (0.4-10.3)
WBC after surgery	4-11×10^9/L	106 (3)	Reference Cat.
	>11×10^9/L	49 (3)	2.2 (0.4-11.5)
	Missing	37 (1)	-
AMP deliveries	Yes	120 (7)	Reference Cat.
	No	72 (0)	-
The duration of AMP deliveries	NO-AMP	72 (0)	-
	≤1day	48 (3)	Reference Cat.
	>1day	72 (4)	0.9 (0.2-4.1)
TCM deliveries	Yes	139 (4)	Reference Cat.
	No	53 (3)	2.0 (0.4-9.4)

Table 5 Demographic characteristics of patients undergoing spinal surgery at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014 (N=192)

Characteristics	SSI(N=7)	Non-SSI(N=185)	*P*-value*
Age at surgery, mean(SD), year	60.3(15.5)	61.8(14.7)	0.553
BMI, mean (SD), kg/m^2	23.6(2.8)	23.1(2.7)	0.273
Duration of operation, mean (SD),minutes	167.1(103.3)	122.5(102.8)	0.499
Total amount of drainage, mean (SD), ml	399.2(307.1)	258.5(185.1)	0.180

**Wilcoxon test* was used for continuous variables

Table 6 Microbiologic characteristics of orthopedic SSI at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014 (N=4)

Microorganism(s)	No. of cases
Escherichia coli + ESBLs	1
Enterobacter cloacae	1
Negative	2
Total	4

** ESBLs: Extended-spectrum beta-lactamases, SSI: Surgical site infection*

8 Discussions

8.1 Incidence proportion of surgical site infection

This study has identified that an incidence proportion of SSI after orthopedic surgery was 2.8% (8/287), from which 3.6% (7/192) developed SSI after spinal surgery in an orthopedic ward of Dong Guan Hospital of Traditional Chinese Medicine.

The incidence of orthopedic SSI identified in this study was comparable to the statistical figures from Chinese national survey[9], but was slightly higher than the figures from ECDC report[15]. We also found that the incidence of spinal orthopedic SSI was slightly higher compared with other types of orthopedic SSI. This finding is consistent with what's reported in the literatures [13, 15].

We suspect that the incidence proportion of SSI identified by this study might be underestimated due to no SSI being detected by PDS. Other studies showed that 1.7%-3.3% of SSIs were detected by PDS [29, 30, 69-71].

A possible explanation for no SSIs being detected during post-discharge was a low attendance at the out-patients clinic for examination of incisional sites. Some patients are living far away from the Dong Guan Hospital of Traditional Chinese Medicine. They might have attended to a hospital

nearby them for checkup or readmission. There was no system that synchronized information enables us to identify SSI among patients in other hospital.

In our study, 72.5% cases completed the phone-interview during post-discharge. The mean age was higher among patients not-interviewed by phone than those being interviewed (59.1 years VS 52.3 years). It is known that elder people had a risk of SSI [32]. It might be that they were SSIs among those not being interviewed.

8.2 Risk factors for spinal surgery

Wound contamination class, wound drains, and blood transfusion were associated with the occurrence of spinal orthopedic SSI in the bivariate analysis. These risk factors are also reported by others [13, 32-34, 72, 73]. Others have identified ASA scores, instrumentation, duration of surgical procedure⩾3h, longer duration of AMP administrated to be association with SSI after spinal surgery. However, in our study, these factors were not associated with SSI. A possible explanation is that the present study was underpowered and therefore unable to identify association between SSI and some variables.

In this study, wound contamination class as a risk factor has association with the occurrence of orthopedic spinal SSI. This finding was consistent with previous studied article [71]. Wound drains were risk factor for orthopedic spinal SSI. This result is consistent with published studies [73, 74]. The longer the drains remained in place, the higher the risk of postoperative wound infection. Drains may increase the risk of infection by causing local tissue inflammation and/or providing direct access to the surgical site for bacteria by ascending the drain tract [73, 75, 76]. Blood transfusion as a risk factors has association with infection after orthopedic spinal surgery, which is consistent with the article published by Ho et al [77]. Blood transfusion recipients were more susceptible to surgical site infection, and blood transfusion both enhances inflammation and suppresses immunity [78].

8.3 Antimicrobials prophylaxis

In the present study, we identified that 61.3% (176/287) of the in-hospital patients were given AMP after orthopedic surgery, from which 62.5% (120/192) of the in-hospital patients were given AMP after orthopedic spinal surgery. To our knowledge, according to the American Society of Health-System Pharmacists Therapeutic Guidelines, AMP is recommended for orthopedic spinal procedures with and without instrumentation[36]. However, Chinese national guideline [37, 38] shows that AMP is not recommended in general, in which there is no detailed and specific recommendation that AMP should be used for orthopedic spinal procedures in China[38]. The only exception to the guideline[37] is that the cases with high risk factors (such as total hip arthroplasty, total knee arthroplasty, instrumentation and other factors among the orthopedic surgeries) are recommended to use AMP.

In addition, we identified a first or second generation cephalosporin of AMP prescription was administered for routine of surgical prophylaxis. This finding was consistent with the recommendations [40, 79] referred by Ministry of Health in China and identified by studied article[80]. However, the mean duration of prophylactic antimicrobials administration was 2.2 days, which exceeded the recommendation to being within 24 hours postoperative period [40, 80].

8.4 Traditional Chinese Medicine

We described the use of TCM, but cannot conclude on its effect to prevent SSI, though the literatures [81, 82] have shown that TCM such as "*Panax notoginseng saponins*" prescribed in this study could induce the biological effects[46] to combat pathogens. To date, there is no scientific evidence that patient being treated with TCM is less likely to develop SSI. However, to our knowledge, this is the first study evaluating the association between the use of TCM and SSI following spinal surgery using a prospective cohort study, and thereafter more relevant researches in this area are needed.

8.5 Microorganism

In the present study, we identified only few microorganisms in the postoperative procedures. To our knowledge, bacteria isolation is recommended before antibiotics administrated according to "Special Rectification Program for the Clinical Application of Antibiotics in 2013"[83] published by Ministry of Health in China. A possible explanation could be that preforming postoperative bacteria isolations to patients without medical insurance coverage is costly, and thereafter it seems likely that healthcare providers prioritized the orthopedic SSI prevention effort in the application of antimicrobials if the cases being threaten by orthopedic SSI.

9 Limitations

A limitation is that the present study was underpowered. A review article suggested that a sample size would be 456 or larger, which is the sample size required to estimate the incidence, given α=0.05, δ=0.02, and expected incidence=5.0% [45]. Also, the result cannot be generalized due to enrolling the cases from only one orthopedic ward. This incidence rate of SSI is therefore not a representative to the entire hospital.

The interviewers were in shortage of techniques and skills to probe the patients to respond to the PDS-questionnaire. In addition, the information bias/recall bias might occur due to phone-interview only being performed up to 30 days post-discharge. The terminologies documented in questionnaire (Annex 10) to the phone-interview might be difficult to understand for some patients as a fact that can influence the authenticity of datasets.

Some studies referred that the nutritional status, hypothermia [84] in intra-operative period, intra-operative supplemental oxygen [85] and preoperative infections (e.g. urinary tract infection) might be association with orthopedic SSI. However, the present study did not include these factors.

This study also did not document the site-observational information regarding intra-operative characteristics such as surgical scrub, surgeon skill/techniques, and temperature and humidity of

operation theatre, which might influence of the quality of intraoperative procedures.

10 Strengths

This study made available information about the burden of SSI and its risk factors in a selected hospital in China using standardized surveillance method. This project also documented the use of TCM, from which was not currently documented in published study.

Many studies are conducted retrospectively [34, 50, 86-88], while in this project we conducted a prospective cohort study focusing on the patients after orthopedic surgery to identify the risk factors associated with SSI.

In this study, most of the answers to the questionnaires (Annex 9) filled by surgeons were completed. Only the variables (body mass index and white blood cell count after surgery) had some missing information.

Finally, this study had used routine data of the surveillance system in the Dong Guan Hospital of Traditional Chinese Medicine and thus established methods for routine evaluations of the work on infection control in the hospital.

11 Recommendations

More studies with appropriated sample size are needed to identify risk factors associated with SSI among people undergoing spinal surgery.

PDS in this hospital should be modified. Nurses should conduct post-discharge guidance that patients can report actively their medical situation of surgical incision if redness, swelling, pain and even purulent occurred. The interviewers in PDS should be trained about how to probe the patients to respond to the PDS-questionnaire.

To the risk factors identified in the present study, nursing care and attention is recommended to be paid particular to patients with wound classified as contaminated or dirty [67]; early drain removal is recommended [76]; careful monitoring of patients and taking close observations during and after administration of a blood transfusion is also recommended[78].

Dong Guan social and health insurance department should increase the health insurance coverage in the city. Medical expenditure in postoperative bacteria isolation is suggested to be covered by the health insurance.

According to the international guideline, we suggest that AMP is administrated for orthopedic spinal procedures with and without instrumentation[36]. The duration of AMP administration should be less than 24 hours [40, 80]. Bacteria isolation is recommended before AMP administration [83].

12 Conclusions

This study has identified that an incidence proportion of SSI after orthopedic surgery was 2.8%, from which 3.6% developed SSI after spinal surgery in an orthopedic ward of Dong Guan Hospital of Traditional Chinese Medicine. Bivariate analysis indicated several significant risk factors, including wound contamination class, wound drains, blood transfusion. Intravenous AMP was given in 176 of 287 (61.3%) after orthopedic surgery. The average duration of AMP administration was 2.2 days (range 1-9 days). Finally, the orthopedic SSI risk factors identified in present study may use to be for reducing the incidence of SSI in the future.

13 Appendices

Annex 1 Criteria for Defining a Surgical Site Infection developed by CDC

Superficial Incisional SSI [67]
Infection occurs within 30 days after the operation *And* infection involves only skin or subcutaneous tissue of the incision *and* at least *one* of the following: 1. Purulent drainage, with or without laboratory confirmation, from the superficial incision. 2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision. 3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat *and* superficial incision is deliberately opened by surgeon, *unless* incision is culture-negative. 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician. Do *not* report the following conditions as SSI: 1. Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration). 2. Infection of an episiotomy or newborn circumcision site. 3. Infected burn wound. 4. Incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI). *Note:* Specific criteria are used for identifying infected episiotomy and circumcision sites and burn wounds.

Deep Incisional SSI
Infection occurs within 30 days after the operation if no implant† is left in place or within 1 year if implant is in place and the infection appears to be related to the operation And infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision and at least one of the following: 1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site. 2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless site is culture-negative. 3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination. 4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

Notes:

1. Report infection that involves both superficial and deep incision sites as deep incisional SSI.
2. Report an organ/space SSI that drains through the incision as a deep incisional SSI.

Organ/Space SSI

Infection occurs within 30 days after the operation if no implant† is left in place or within 1 year if implant is in place and the infection appears to be related to the operation

And

infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

1. Purulent drainage from a drain that is placed through a stab wound‡ into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

Annex 2 Wound contamination class

Wound contamination class as described by Altemeier et al. [4, 52, 67].

Wound contamination classification

Wound Contamination class	Description
W1	**A clean wound** is an uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow non-penetrating trauma should be included in this category.
W2	**Clean-contaminated wounds** are operative wounds in which the respiratory, alimentary, genital or uninfected urinary tracts are entered under controlled condition and without unusual contamination. Specifically operations involving the biliary tract, appendix, vagina and oropharynx are included in this category provided no evidence of infection or major break in technique is encountered.
W3	**Contaminated wounds** include open, fresh, accidental wounds. In addition operations with major breaks in sterile technique or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered are included in this category.
W4	**Dirty or infected wounds** include old traumatic wounds with retained devitalised tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

Annex 3 The American Society of Anesthesiology physical status classifications

Physical status classification developed by the American Society of Anesthesiology (ASA) [52, 67, 89].

ASA physical status classification

ASA score	Description
A1	Normally healthy patient
A2	Patient with mild systemic disease
A3	Patient with severe systemic disease that is not incapacitating
A4	Patient with an incapacitating systemic disease that is a constant threat to life
A5	Moribund patient who is not expected to survive for 24 hours with or without operation

Annex 4 Wound bacterial cultures

Common Pathogens by Orthopedic surgery [4, 20]

Operation	Likely Pathogens*
Total joint replacement	a. *Gram-positive cocci*: *Staphylococcus aureus*; *Coagulase-negative Staphylococci*
Closed fractures/use of nails, bone plates,	b. *Gram-negative bacilli*
Other internal fixation devices	c. *Enterobacteriaceae*
Functional repair without implant/device	d. Gram-negative bacilli: *Acinetobacter baumannii; Pseudomonadaceae*
Trauma	
Spinal surgery	*e. Staphylococcus aureus, coagulase-negative staphylococci and Pseudomonas aeruginosa.*

*Likely pathogens from both endogenous and exogenous sources.

Annex 5 Antimicrobial prophylaxes

Recommended Doses and Re-dosing Intervals for Commonly Used Antimicrobials for Surgical Prophylaxis from ASHP Guidelines [36]

Recommended Dose			Half-life in Adults With Normal Renal Function, hr	Recommended Redosing Interval (From Initiation of Preoperative Dose), hr [c]
Antimicrobial	Adults [a]	Pediatrics [b]		
Ampicillin	2 g	50 mg/kg	1–1.9	2
Aztreonam	2 g	30 mg/kg	1.3–2.4	4
Cefazolin	2 g, 3 g for pts weighing≥120 kg	30 mg/kg	1.2–2.2	4
Cefuroxime	1.5 g	50 mg/kg	1–2	4
Cefotaxime	1 g [d]	50 mg/kg	0.9–1.7	3
Cefoxitin	2 g	40 mg/kg	0.7–1.1	2
Cefotetan	2 g	40 mg/kg	2.8–4.6	6
Ceftriaxone	2g [e]	50-75 mg/kg	5.4-10.9	NA
Ciprofloxacin [f]	400mg	10mg/kg	3-7	NA
Clindamycin	900mg	10mg/kg	2-4	6
Ertapenem	1g	15mg/kg	3-5	NA
Fluconazole	400mg	6 mg/kg	30	NA
Gentamicin [g]	5 mg/kg based on dosing weight (single dose)	2.5 mg/kg based on dosing weight	2-3	NA
Levofloxacin [f]	500mg	10mg/kg	6-8	NA
Piperacillin–tazobactam	3.375 g	Infants 2–9 mo: 80 mg/kg of the piperacillin component	0.7-1.2	2
Vancomycin	15 mg/kg	15 mg/kg	4–8	NA

a Adult doses are obtained from the studies cited in each section. When doses differed between studies, expert opinion used the most-often recommended dose.

b The maximum pediatric dose should not exceed the usual adult dose.

c For antimicrobials with a short half-life (e.g., cefazolin, cefoxitin) used before long procedures, redosing in the operating room is recommended at an interval of approximately two times the half-life of the agent in patients with normal renal function. Recommended redosing intervals marked as ‘‘not applicable’’ (NA) are based on typical case length; for unusually long procedures, redosing may be needed.

d Although FDA-approved package insert labeling indicates 1g,14 experts recommend 2g for obese patients.

e When used as a single dose in combination with metronidazole for colorectal procedures.

f While fluoroquinolones have been associated with an increased risk of tendinitis/tendon rupture in all ages, use of these agents for single-dose prophylaxis is generally safe.

g In general, gentamicin for surgical antibiotic prophylaxis should be limited to a single dose given preoperatively. Dosing is based on the patient’s actual body weight. If the patient’s actual weight is more than 20% above ideal body weight (IBW), the dosing weight (DW) can be determined as follows: DW = IBW + 0.4(actual weight – IBW).

Annex 6 Definition of the variables included for surveillance of surgical site infection

Patients characteristics	Definition of the variables [52, 67]
Age	Age at date of operation in years
Date of hospital admission (Day)	Date patient was admitted to hospital in order to undergo the operation under surveillance (YYYY-MM-DD).
Gender	The gender of the patient who undergoes the operation: M = Male, F = Female.
BMI[90]	BMI＞25 kg/m^2, BMI≤25 kg/m^2
ASA score	Annex 3
Diabetes mellitus [91]	Yes= Either fasting plasma glucose ≥ 7.0 mmol /l (126 mg/dl) or with a glucose tolerance test, two hours after the oral dose a plasma glucose ≥ 11.1 mmol/l (200 mg/dl). Otherwise =No
Rheumatoid arthritis[92]	Yes= X-rays of joints and blood test results are abnormal.
Bone oncology[93]	Yes= Bone imaging (clinical and skeletal interventional radiology), bone biomarkers (clinical and translational applications), skeletal complications, and bone pain (mechanisms and management). Otherwise =No
Pre-operative stay	The number of days from hospital admission to the day of the operation the patient is enrolled into the study for.
Orthopedic instrumentation	An orthopedic instrumentation is a device surgically placed into the body designed to restore function by replacing or reinforcing a damaged structure.
Operation ICD-9-CM code of orthopedic surgery	Defines in accordance with the standardized ICD-9-CM code
Urgent operation	Planning time of the operation. ‘Yes’ means urgent operation that was not planned at least 24 hours in advance. ‘No’ means elective operation that was planned at least 24 hours in advance. Y =Yes (urgent), N = No (elective), UNK = Unknown.

Skin preparation [94]	Yes=skin preparation using chlorhexidine-, povidone-, iodine-based preparations. Otherwise =No
Date of operation (Day)	Date operation under surveillance was carried out (YYYY-MM-DD).
Wound contamination class	The wound contamination class as described in Annex 2: W1= Clean, W2 = Clean-contaminated, W3 = Contaminated, W4 = Dirty or infected, UNK = Unknown. (Annex 2)
Duration of operation in minutes	Duration of operation (in minutes) from skin incision to skin closure. In case of re-intervention within 72h after the primary procedure, the duration of the re-intervention is added to the duration of the primary procedure.
The number participants in the orthopedic surgery	Mark how many participants attend in the orthopedic surgery.
Intraoperative blood loss	Mark how many milliliter loss of blood during a surgical procedure.
Date of discharge (Days)	Date the patient was discharged from hospital where they underwent the operation under surveillance or date of in-hospital death. This date is used to calculate the number of post-operative in-hospital patient days.
Wound bacterial cultures	Annex 4
White blood cell count	The reference ranges index of WBC is 4~11×10^9/L for adult.
Intraoperative blood transfusion	The introduction of whole blood or blood component directly into the blood stream during the surgical procedure.
Drains	Yes= that a drain to remove fluids or discharges from the body, such as from a wound, sore, or cavity was inserted. Otherwise =no
Date of last follow-up post-discharge	Date last information on the patient was obtained after discharge from hospital, for example from surgeon (out-patient department or private practice) or general practitioner. This date is used to calculate the total amount of follow-up days (in-hospital and post-discharge) (YYYY-MM-DD).
Antimicrobial prophylaxis	Perioperative systemic administration of antimicrobial agent(s) at or within two hours prior to primary skin incision with the aim of preventing sepsis in the

	operative site. Y =Yes (patient received surgical antimicrobial prophylaxis), N= No (patient did not receive surgical antimicrobial prophylaxis), UNK = Unknown. (Annex 5)
Traditional Chinese Medicine	TCM was documented to have biological effects on limb swelling and tissue healing and to be anti-inflammatory, promoting circulation and supporting tissue/bone healing. Y =Yes (patient received TCM after orthopedic surgery), N= No (patient did not receive TCM after orthopedic surgery), UNK = Unknown.
Surgical Site Infection	Presence of a surgical site infection for this operation (Annex1).
Date of infection	Date when the first clinical evidence of SSI appeared or the date the specimen used to make or confirm the diagnosis was collected, whichever comes first (YYYY-MM-DD).
Type of Infection	Type of infection (Annex1). S = Superficial incisional, D = Deep incisional, O = Organ/space, UNK = Unknown.

Annex 7 Definition of incidence rate of orthopaedic spinal SSI and its possible risk factors

Name of surgical procedures	Incidence rate of SSI	Possible risk factors
Vertebroplasty	1%-3.7% [95, 96]	ASA score, BMI, older age, longer operative time, and length of stay [95, 97, 98]
Spinal decompression	2.4%-8.6% [99-103]	ASA score, BMI, diabetes, blood loss, and longer operative time [99, 104-107]
Spinal fusions	0.74%-4.4% [108-111]	ASA score greater than 2, obesity, diabetes, longer operative time, orthopedic implant and prolonged duration of drains [72, 73, 111-113]

Annex 8 Specific functions of common traditional Chinese medicine constituents

Common TCM constituents	Specific functions
Panax notoginseng saponins	Promote blood circulation, anti-inflammatory and analgesic activity, immunological adjuvant activity and immune-stimulatory action, and hemostatic activity[62].
Salvia miltiorrhiza	Increase blood flow and promote blood circulation[114].
Lumbricus rubellus	Promote blood circulation[115].

Annex 9 The questionnaire for patients with orthopedic surgery

Please fill in data for each patient who had surgery

Admission Number (AD):		Age:		Gender:
Date of hospital admission:				
Weight(KG):		Height(CM):		BMI=
Hypertension: Yes or No or Unknown			Diabetes mellitus (DM): Yes or No or Unknown	
Rheumatoid arthritis (RA): Yes or No or Unknown			Bone oncology: Yes or No or Unknown	
Main Diagnosis:			Date of operation:	
Type of orthopedic surgery:			ICD-9-CM code:	
ASA score： A1 A2 A3 A4 A5			Would contamination class: C1 C2 C3 C4	
Skin preparation: Yes or No or Unknown			Urgent operation: Yes or No or Unknown	
Instruments: Yes or No or Unknown			Duration of operation in minutes:	
Orthopedic surgeries operation room NO. :				
The number of participants in the orthopedic surgery:				
Intraoperative blood Loss(ml)			Drainage: Yes or No or Unknown	
Duration of drainage (Days):			Total amount of drainage (ml):	
Intraoperative blood transfusion: Yes or No or Unknown			Pre-operative staying:	
Antibiotic prophylaxis: Yes or No or Unknown			Traditional Chinese Medicine: Yes or No or Unknown	
Type of AMP	Dose	Time of first dose	Regime	Time of last dose
Type of CM	Dose	Time of first dose	Regime	Time of last dose
Surgical Site Infection: Yes or No			Type of SSI:	
Date of infection:			WBC: Normal or Abnormal or Unknown	
Isolate result:			Antibiotic Resistance data:	
Date of discharge from the hospital (Day):			Doctor signature:	

Annex 10 The questionnaires for the patients discharge after 30 days of surgery

Has green/yellow pus discharged from your surgical wound? **Yes or No**
Has the area around your surgical wound been unusually red (more than ½ cm on each side)? **Yes or No**
Has a doctor (physician) opened the wound because of infection? **Yes or No**
Have you received antibiotic treatment because of infection in the surgical wound? **Yes or No**
Have you had a fever (above 38.5 °C) because of infection in the surgical wound? **Yes or No**
OTHER
Date of last follow-up post-discharge:
Surgical Site Infection: **Yes or No**
Type of SSI:
Date of infection:

*For telephone interview

Annex 11 Ethical Clearances in Norway

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Vivi Opdal	22845526	23.05.2014	2014/650/REK sør-øst A
			Deres dato:	Deres referanse:
			08.04.2014	

Vår referanse må oppgis ved alle henvendelser

Hanne-Merete Eriksen
Nasjonalt folkehelseinstitutt

2014/650 Healthcare-associated infections (HAIs) after orthopedic surgery performed in Dong Guan hospital of Traditional Chinese Medicine (TCM) in China

Forskningsansvarlig: Nasjonalt folkehelseinstitutt
Prosjektleder: Hanne-Merete Eriksen

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) A i møtet den 08.05.2014. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikklovens § 4.

Prosjektbeskrivelse

Formålet med prosjektet er å undersøke omfanget av infeksjoner i operasjonssår og risikofaktorer blant pasienter som undergår ortopediske operasjoner ved Dong Guan sykehuset i Kina for å vurdere kvaliteten på tilbudet og forbedre pasientsikkerheten. I prosjektet er det planlagt å benytte data registrert i sykehusets kvalitetssikringssystem. I tillegg planlegges det å gjennomføre et telefonintervju av pasienter som har gjennomgått ortopediske operasjoner 30 dager etter utskrivelse for å undersøke om det har oppstått infeksjon i operasjonssåret. Videre skal man forsøke å registrere pasienter som blir re-innlagt på grunn av infeksjoner samt registrere eventuelle infeksjoner som håndteres ved poliklinikk. Det skal også samles inn opplysninger om bruken av tradisjonell kinesisk medisin i kombinasjon med profylaktisk bruk av antibiotika skal. Det er ikke planlagt å innhente samtykke for å analysere dataene som rutinemessig registreres i sykehusets kvalitetssikringssystem. Det skal imidlertid innhentes informert samtykke for intervjudataene som innhentes etter utskriving. Populasjonen er alle pasienter som undergår en ortopedisk operasjon på en gitt avdeling i tidsrommet juni til november 2014, omlag 150-200 pasienter. Medisinsk personell skal gis opplæring i klassifiseringen av infeksjoner og i innhentingen av data til kvalitetssikringssystemet for å foreta daglige undersøkelser av operasjonssår og evaluere pasientjournalene.

Komiteens vurdering

Etter komiteens vurdering er deler av prosjektet kvalitetssikring av gitt behandling. Det skal ikke foretas noen undersøkelser eller inngripen i pasientenes behandling, men en stund etter sykehusoppholdet skal man kontakte dem og spørre om hvordan det har gått. Etter en helhetsvurdering har komiteen kommet til at prosjektet anses som medisinsk og helsefaglig forskning, som dermed er fremleggingspliktig for REK. Komiteen finner at prosjektet, slik det er beskrevet, er å anse som forsvarlig å gjennomføre.

Helseforskningsloven gjelder også medisinsk og helsefaglig forskning i utlandet når forskningen skjer i regi av en forskningsansvarlig som er etablert i Norge. Slik forskning skal dermed godkjennes av REK i Norge.

Besøksadresse:
Gullhaugveien 1-3, 0484 Oslo

Telefon: 22845511
E-post: post@helseforskning.etikkom.no
Web: http://helseforskning.etikkom.no/

All post og e-post som inngår i saksbehandlingen, bes adressert til REK sør-øst og ikke til enkelte personer

Kindly address all mail and e-mails to the Regional Ethics Committee, REK sør-øst, not to individual staff

Hensikten er å unngå at risikofylt forskning flyttes til u-land med ikke-eksisterende eller dårligere regulering av forskning, med den følge at internasjonalt anerkjente prinsipper ikke overholdes og/eller at forskningsdeltakere blir utilbørlig utnyttet eller utsatt for uakseptabel risiko og ulempe.

REK kan imidlertid bare gi en godkjenning for prosjektet som sådan, og kan ikke gi dispensasjon fra taushetsplikten til å samle inn opplysninger fra journaler ved Dong Guan sykehuset i Kina som er bindende for det aktuelle sykehuset. Det forutsettes derfor at det søkes om nødvendige stedlige godkjenninger for å gjennomføre prosjektet, herunder tillatelse til å samle inn opplysninger fra sykehusets kvalitetssikringssystem.

Vedtak

Komiteen godkjenner prosjektet i henhold til helseforskningsloven § 9 og § 33 under forutsetning av at nødvendige stedlige godkjenninger innhentes.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Godkjenningen gjelder til 30.11.2014.

Av dokumentasjonshensyn skal opplysningene oppbevares i 5 år etter prosjektslutt. Opplysningene skal oppbevares avidentifisert, dvs. atskilt i en nøkkel- og en datafil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse- og omsorgssektoren».

Prosjektet skal sende sluttmelding på eget skjema, jf. helseforskningsloven § 12, senest et halvt år etter prosjektslutt.

Dersom det skal gjøres endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK, jf. helseforskningsloven § 11.

Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jf. helseforskningsloven § 10 tredje ledd og forvaltningsloven § 28. En eventuell klage sendes til REK sør-øst A. Klagefristen er tre uker fra mottak av dette brevet, jf. forvaltningsloven § 29.

Med vennlig hilsen

Knut Engedal
Professor dr. med.
Leder

Vivi Opdal
seniorrådgiver

Kopi til: *hmer@fhi.no; folkehelseinstituttet@fhi.no*

Annex 12 Ethical Clearances in China

东莞市中医院关于开展“外科手术部位感染”医学伦理委员会审批表

项目名称：	外科手术部位感染的流行病学现状与相关危险因素的研究		
项目类型	☐药物 ☐器械 ☑其他		
申请专业	院内感染	主要研究者	王建聪
课题承办机构	东莞市中医院		
会议审查资料	审核资料目录：（见附表）	审查类别	会议审查
会议日期	2014 年 6 月 15 日	会议地点	行政楼三楼会议室

伦理委员会委员名单及到会委员签名

职务	姓名	性别	职称	从事专业	单位	签名
主委	郑志文	男	副教授	中医内科	东莞市中医院	
副主委	蔡立民	男	教授	中医骨伤科	东莞市中医院	
委员	何仲佳	男	教授	中医骨伤科	东莞市中医院	
委员	董明国	男	教授	脾胃病科	东莞市中医院	
委员	宁为民	女	教授	神经内科	东莞市中医院	
委员	周咏梅	女	教授	护理学	东莞市中医院	
委员	周顺良	男	教授	中医内科	东莞市人民医院	
委员	罗建东	男	助理档案馆员	法医学	东莞市中医院	

伦理委员会人数 8 人	出席人数 8 人	缺席人数 0 人	回避人数 0 人

投票结果	同意	作必要修正后同意	作必要修正后重审	不同意	终止或暂停试验	回避
	8 票	票	票	票	票	票

备注：1=I 期临床试验；2=II 期临床试验；3=III期临床试验；4=IV临床试验；
5=进口药品注册；6=器械监试试验；7=其它

地址：东莞市松山湖大道 22 号 邮编：523000 联系人：王建聪 联系电话：0769-26385528

伦理委员会审查意见：

1、经东莞市中医院医学伦理委员会审查，“外科手术部位感染的流行病学现状与相关危险因素的研究”项目审查材料齐全、经充分讨论、满足法定到会人数，符合《人体对象医学研究的道德原则》（赫尔辛基宣言）。

2.该项研究鉴于可能会涉及到医院行政管理的数据，研究者需在数据采集与发表中有意识规避医院行政管理的风险点，并保护受试者的隐私和数据的机密性。

3. 开展该研究，受试者和目标人群均可获益，不但有助于提高医务人员的院感防控意识，而且能早期发现与外科手术部位感染相关的危险因素，给予早期的干预，从而能达到更好地预防与控制外科手术部位感染的效果。

同意进行该项研究。

主任委员签名：

（盖章）

2014 年 6 月 15 日

注意：

1.如发生严重不良事件，请在获知后 24 小时内报告至伦理委员会。

2.如修改研究方案及相关材料，请及时上报伦理委员会。

3.如为跨年度研究，请及时将年度报告提交至伦理委员会。

4.无论开始与否，请在持续审查到期前 1 个月提出持续审查的申请。

5.完成临床研究，须提交结题报告供伦理委员会审查。

声明：

本伦理委员会按照《中医药临床研究伦理审查管理规范》组成和工作，其审查和工作过程不受伦理审查委员会以外任何组织及个人的影响。

Annex 13 Ethical Clearances in China (Translation version)

Approval Form of Ethical Clearances

by the Committee of Dong Guan Hospital of Traditional Chinese Medicine (TCM)

Project Name:	Healthcare-associated infections (HAIs) after orthopedic surgery performed in Dong Guan hospital of Traditional Chinese Medicine (TCM) in China		
Project Type	□ Drug □ Instrument √ Others		
Professional areas	Nosocomial infection	Principal Investigator	Jiancong Wang
Review materials	Research Protocol	Review type	Conference review
Conference Date	June 15, 2014	Conference Location	Conference room

List of the Ethical Committee Members and signatures of the present committee members

Position	Name	Sex	Title	Profession	Unit	Signature：
Chairman	Zheng Zhiwen	Male	Associate Professor	Traditional Chinese medicine	Dongguan Hospital of TCM	Zheng Zhiwen
Vice Chairman	Cai Limin	Male	Professor	Orthopedics	Dongguan Hospital of TCM	Cai Limin
Committee Members	He Zhongjia	Male	Professor	Orthopedics	Dongguan Hospital of TCM	He Zhongjia
Committee Members	Dong Mingguo	Male	Professor	Gastroenterology	Dongguan Hospital of TCM	Dong Mingguo
Committee Members	Ning Weimin	Female	Professor	Neurology	Dongguan Hospital of TCM	Ning Weimin
Committee Member	Zhou Yongmei	Female	Professor	Nursing	Dongguan Hospital of TCM	Zhou Yongmei
Committee Member	Zhou Shunliang	Male	Professor	Traditional Chinese medicine	Dongguan People's Hospital	Zhou Shunliang
Committee Member	Luo Jiandong	Male	Assistant archivist	Forensic medicine	Dongguan Hospital of TCM	Luo Jiandong
Number of Ethical Committee Members: 8			Attendance: 8		Absence: 0	Withdraw: 0

Voting result	Supporting votes: 8	Supporting votes after necessary amendments: 0	Votes for review after necessary amendments: 0	Disagree votes: 0	Votes for termination or suspension of the test: 0	Votes of withdraw: 0

Remark: 1 = I clinical trial ; 2 = II clinical trial ; 3 = III clinical trial 4 = IV clinical trial
5=imported drug registration; 6=instrument monitoring test; 7=others

Address: No.22 Song Shan Lake Avenue, Dongguan, China. Zip Code: 523000

Contact: Jiancong Wang Tel: 0769-26385528

Review Comments of the Ethical Committee:

1. By the review of the Medical Ethics Committee of Dongguan Hospital of Traditional Chinese Medicine, the project review materials of Research on "Healthcare-associated infections (HAIs) after orthopedic surgery performed in Dong Guan hospital of Traditional Chinese Medicine" are approved. After discussion, it meets the quorum and conforms to the Ethical Principle of Human Subject Medical Research (Declaration of Helsinki).
2. Given that this research may be related to the hospital administrative data, the researchers need to consciously avoid the risk of the hospital administration and protect the privacy and confidentiality of the participants in the data collection and data disclosure.
3. This research may benefit both the subjects and the target population, help the medical staff improve the prevention and control consciousness of hospital infection and timely find the related risk factors of surgical site infections so as to give early intervention and achieve better prevention and control of surgical site infections.

Agree to conduct this research.

Signature of Chairman

Zhiwen Zheng(Seal)

June 15, 2014

Attention:

1. In the case of serious adverse events, please report it to the Ethical Committee within 24 hours after informed.
2. Any change to the research proposal and the related materials need to be promptly reported to the Ethical Committee.
3. As for the inter-annual research, please report to the Ethical Committee.
4. Please apply for the re-review, if the research project will be incomplete before the expiration day.
5. To complete the clinical researches, please submit the concluding report to the Ethical Committee for review.

Statement:

The Ethical Committee will be established and operated in accordance with the Management Standard for Clinical Research Ethical Review of Traditional Chinese Medicine. The outcome of review and work process would not be influenced by any organization or individual outside the Ethical Committee.

Annex 14 Supporting letter from the University of Oslo

UiO : Faculty of Medicine
University of Oslo

To whom it may concern

Oslo 02.04.2014
Your ref.:
Our ref.: Terese Eriksen

Supporting letter for Jiancong Wang

We hereby confirm that Jiancong Wang, born on November 24th 1983 and passport ID number G40323284, is enrolled as a fulltime master student at our two year M.Phil program in International Community Health at the University of Oslo. He was admitted in August 2013, and is expected to complete his degree in the spring of 2015. Wang has this far made a steady progress in his studies and completed all his examinations according to plan.

It is a requirement of this master program that the students develop and conduct a research project in the area of their choice within the field of international community health. As an epidemiologist, Jiancong Wang has developed a research project with the working title of "Reducing healthcare-associated infections (HAIs) after orthopedic surgery performed in Dong Guan hospital of Traditional Chinese Medicine (TCM)". He would like to conduct his fieldwork and collect data in the Dong Guan hospital of Traditional Chinese Medicine from July 1st to the December 31st 2014.

In Norway Jiancong Wang has the support of his supervisors Professor Gunnar Bjune at the Institute of Health and Society at University of Oslo and senior advisor Hanne Merete Eriksen (PhD) at The Norwegian Institute of Public Health.

We hope that permission will be granted.

For any questions or need for clarification please contact us.

Sincerely yours

Terese Eriksen

Terese Eriksen
Program Coordinator
Master program in International Community Health
Phone: + 47 22 85 05 26
Email: terese.eriksen@medisin.uio.no

M.PHIL PROGRAMME
INTERNATIONAL COMMUNITY HEALTH
FACULTY OF MEDICINE
UNIVERSITY OF OSLO, NORWAY

Institute of Health and Society
Department of Community Medicine
Postal addr.: PO Box 1130 Blindern, 0318 Oslo
Visiting addr.: Frederik Holsts hus, Kirkeveien 166, 0850 Oslo

Phone: (+47) 22 85 05 50
Telefax: (+47) 22 85 05 90
postmottak@medisin.uio.no
www.med.uio.no/helsam
Org. no.: 971 035 854

14 References

1. Bates, D.W., et al., *Global priorities for patient safety research.* Bmj, 2009. **338**: p. b1775.
2. Burke, J.P., *Infection control - a problem for patient safety.* N Engl J Med, 2003. **348**(7): p. 651-6.
3. Allegranzi, B., et al., *Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis.* Lancet, 2011. **377**(9761): p. 228-41.
4. Reichman, D.E. and J.A. Greenberg, *Reducing surgical site infections: a review.* Rev Obstet Gynecol, 2009. **2**(4): p. 212-21.
5. *Report on the Burden of Endemic Health Care-Associated Infection Worldwide.* World Health Organization 2011, 2011. **Available on: http://apps.who.int/iris/bitstream/10665/80135/1/9789241501507_eng.pdf?ua=1**.
6. Stoesser, N., et al., *The value of intermittent point-prevalence surveys of healthcare-associated infections for evaluating infection control interventions at Angkor Hospital for Children, Siem Reap, Cambodia.* Trans R Soc Trop Med Hyg, 2013. **107**(4): p. 248-53.
7. Kumar, A., et al., *Point prevalence surveys of healthcare-associated infections and use of indwelling devices and antimicrobials over three years in a tertiary care hospital in India.* J Hosp Infect, 2014. **86**(4): p. 272-4.
8. Thu, T.A., et al., *A point-prevalence study on healthcare-associated infections in Vietnam: public health implications.* Infect Control Hosp Epidemiol, 2011. **32**(10): p. 1039-41.
9. WU An-hua, W.X.-m., LI Chun-hui,REN Nan,GONG Ru-e,HUANG Xun,FENG Li,LIU Zhen-ru,MENG Li,GUO Yan-hong, *China national point prevalence survey on healthcare-associated infection and antimicrobial use in 2012.* Chinese Journal of Infection Control, 2014(01): p. 8-15.
10. WU An-hua, R.N., WEN Xi-mao, YI Xia-yun, HUANG Xun, XU Xiu-hua, *One-day prevalence survey of nosocomial infection in 159 hospitals.* Chinese Journal of Infection Control, 2005(01): p. 12-17.
11. Wu An-hua, R.N., Wen Xi-mao, Yi Xia-yun, Huang Xun, Xu Xiu-hua, Gong Yu-xiu *A Nosocomial Infection Point-Prevalence Survey: Results and Analysis of 193 Hospitals in China in 2001.* Chinese Journal of Nosoconmiology, 2002(08): p. 6-8.
12. Ogihara, S., et al., *Prospective multicenter surveillance and risk factor analysis of deep surgical site infection after posterior thoracic and/or lumbar spinal surgery in adults.* J Orthop Sci, 2015. **20**(1): p. 71-7.
13. Xing, D., et al., *A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery.* Eur Spine J, 2013. **22**(3): p. 605-15.
14. *Surveillance of surgical site infections in Europe, 2011 Based on surveillance data of 2008 and 2009.* European Centre for Disease Prevention and Control, 2011. **Available at: http://www.ecdc.europa.eu/en/publications/Publications/120215_SUR_SSI_2008-2009.pdf**.
15. Zarb, P., et al., *The European Centre for Disease Prevention and Control (ECDC) pilot point prevalence survey of healthcare-associated infections and antimicrobial use.* Euro Surveill, 2012. **17**(46).
16. Korol, E., et al., *A systematic review of risk factors associated with surgical site infections among surgical patients.* PLoS One, 2013. **8**(12): p. e83743.
17. Leaper, D.J., et al., *Surgical site infection - a European perspective of incidence and economic burden.* Int Wound J, 2004. **1**(4): p. 247-73.
18. Kassavin, D.S., L. Pascarella, and M.A. Goldfarb, *Surgical site infections: incidence and trends at a community teaching hospital.* Am J Surg, 2011. **201**(6): p. 749-53.
19. Caputo, A.M., et al., *Risk factors for infection after orthopaedic spine surgery at a high-volume institution.* J Surg Orthop Adv, 2013. **22**(4): p. 295-8.
20. Mackenzie, W.G., et al., *Surgical site infection following spinal instrumentation for scoliosis: a multicenter*

analysis of rates, risk factors, and pathogens. J Bone Joint Surg Am, 2013. **95**(9): p. 800-6, s1-2.

21. Kakimaru, H., et al., *Postoperative antimicrobial prophylaxis following spinal decompression surgery: is it necessary?* J Orthop Sci, 2010. **15**(3): p. 305-9.
22. Lee, J., et al., *Surgical site infection in the elderly following orthopaedic surgery. Risk factors and outcomes.* J Bone Joint Surg Am, 2006. **88**(8): p. 1705-12.
23. Nie, H., et al., *Procalcitonin as an early predictor of postoperative infectious complications in patients with acute traumatic spinal cord injury.* Spinal Cord, 2011. **49**(6): p. 715-20.
24. XU Hai-li, N.L.-d., YE Qian-qian, XU Hua-zi, LI Xiao-cong, *Related factors for postoperative incisional infections in patients undergoing spinal surgery.* Chinese Journal of Nosocomiology, 2015.
25. LIN Qing-song, Z.Z.-m., CHEN Jian-ting, *Risk factors for surgical site infections after spine surgery.* The Journal of Practical Medicine,, 2014.
26. *Hospital Management Assessment Guideline (Version 2008).* 2008. **Available at: http://www.moh.gov.cn/mohyzs/s3585/200806/36242.shtml**.
27. ZHONG Qun-jie, L.J.-h., WU Ying-hong, *Targeted monitoring of surgical site infections after total hip arthroplasty in Beijing in 2010.* Chinese Journal of Nosocomiology, 2012(16): p. 3517-3520.
28. XIE Zhang-jia, P.A.-q., XIE Zhuang, *Risk factors of early surgical site infection after total hip arthroplasty.* Chinese Journal of Joint Surgery(Electronic Edition), 2011(04): p. 446-450.
29. Kent, P., et al., *Post-discharge surgical wound infection surveillance in a provincial hospital: follow-up rates, validity of data and review of the literature.* ANZ J Surg, 2001. **71**(10): p. 583-9.
30. Rosenthal, R., et al., *Surveillance of surgical site infections by surgeons: biased underreporting or useful epidemiological data?* J Hosp Infect, 2010. **75**(3): p. 178-82.
31. Reilly, J., et al., *Procedure-specific surgical site infection rates and postdischarge surveillance in Scotland.* Infect Control Hosp Epidemiol, 2006. **27**(12): p. 1318-23.
32. Pull ter Gunne, A.F., et al., *A methodological systematic review on surgical site infections following spinal surgery: part 1: risk factors.* Spine (Phila Pa 1976), 2012. **37**(24): p. 2017-33.
33. Radcliff, K.E., et al., *Preoperative delay of more than 1 hour increases the risk of surgical site infection.* Spine (Phila Pa 1976), 2013. **38**(15): p. 1318-23.
34. Pull ter Gunne, A.F. and D.B. Cohen, *Incidence, prevalence, and analysis of risk factors for surgical site infection following adult spinal surgery.* Spine (Phila Pa 1976), 2009. **34**(13): p. 1422-8.
35. Yang, Z., et al., *DRUGS system enhancing adherence of Chinese surgeons to antibiotic use guidelines during perioperative period.* PLoS One, 2014. **9**(8): p. e102226.
36. *Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery.* ASHP Therapeutic Guidelines, 2013. **Available at: http://www.ashp.org/surgical-guidelines**.
37. *National Health & Family Planning Commission, P.R.China. Principle guideline for antimicrobials clinical use. Beijing. Available at http://www.moh.gov.cn/mohyzs/s3573/200804/18544.shtml.*
38. Sun, J., *Systematic review of interventions on antibiotic prophylaxis in surgery in Chinese hospitals during 2000-2012.* J Evid Based Med, 2013. **6**(3): p. 126-35.
39. Li, G.H., et al., *A review of prophylactic antibiotics use in plastic surgery in China and a systematic review.* Int J Surg, 2014. **12**(12): p. 1300-5.
40. National Health & Family Planning Commission, P.R.C., *Principle guideline for antimicrobials clinical use.* Available at: http://www.moh.gov.cn/mohyzs/s3573/200804/18544.shtml.
41. Rodriguez-Merchan, E.C., *Preventing surgical site infection in haemophilia patients undergoing total knee arthroplasty.* Blood Coagul Fibrinolysis, 2012. **23**(6): p. 477-81.

42. Koutsoumbelis, S., et al., *Risk factors for postoperative infection following posterior lumbar instrumented arthrodesis.* J Bone Joint Surg Am, 2011. **93**(17): p. 1627-33.
43. Li, G.Q., et al., *Epidemiology and outcomes of surgical site infections following orthopedic surgery.* Am J Infect Control, 2013. **41**(12): p. 1268-71.
44. Roy, M.C. and T.M. Perl, *Basics of surgical-site infection surveillance.* Infect Control Hosp Epidemiol, 1997. **18**(9): p. 659-68.
45. Fan, Y., et al., *The incidence and distribution of surgical site infection in mainland China: a meta-analysis of 84 prospective observational studies.* Sci Rep, 2014. **4**: p. 6783.
46. Tan, B.K. and J. Vanitha, *Immunomodulatory and antimicrobial effects of some traditional chinese medicinal herbs: a review.* Curr Med Chem, 2004. **11**(11): p. 1423-30.
47. Leung, P.C., *Traditional Chinese Medicine and orthopaedics-is there room for modern application?* Chin Med J (Engl), 2012. **125**(22): p. 3931-8.
48. Leung, P.-C., *Traditional Chinese Medicine in orthopaedics—Problems and future direction.* Open Journal of Therapy and Rehabilitation, 2014. **02**(01): p. 1-4.
49. Lonjon, G., et al., *Early surgical site infections in adult spinal trauma: a prospective, multicentre study of infection rates and risk factors.* Orthop Traumatol Surg Res, 2012. **98**(7): p. 788-94.
50. Namba, R.S., M.C. Inacio, and E.W. Paxton, *Risk factors associated with surgical site infection in 30,491 primary total hip replacements.* J Bone Joint Surg Br, 2012. **94**(10): p. 1330-8.
51. Cies, J.J., et al., *Influence of body mass index and antibiotic dose on the risk of surgical site infections in pediatric clean orthopedic surgery.* Surg Infect (Larchmt), 2012. **13**(6): p. 371-6.
52. *Surveillance of surgical site infections in European hospitals – HAISSI protocol. Version 1.02.* European Centre for Disease Prevention and Control, 2012. **Available at: http://www.ecdc.europa.eu/en/publications/Publications/120215_TED_SSI_protocol.pdf**.
53. Dubory, A., et al., *Surgical-site infection in spinal injury: incidence and risk factors in a prospective cohort of 518 patients.* Eur Spine J, 2014.
54. *The Dong Guan City National Economic and Social Development statistics in 2011.* Available on: http://www.dgs.gov.cn/website/flaArticle/art_show.html?code=nj2012&fcount=2, 2011.
55. *GDP per capita in Norway.* Available at: http://data.worldbank.org/indicator/NY.GDP.PCAP.CD, 2013.
56. *the Health Bureau of Dong Guan City.* Available on: http://www.dgwsj.gov.cn/publicfiles/business/htmlfiles/ewsj/index.htm.
57. *Nosocomial Infectious Control Measurement.* The official web on the Central People's Government of the PRC, 2006. **http://www.gov.cn/ziliao/flfg/2006-07/25/content_344886.htm**.
58. *Standard for nosocomial infection surveillance WS/T312-2009.* Available on: http://wsb.moh.gov.cn/cmsresources/mohylfwjgs/cmsrsdocument/doc6110.pdf, 2009.
59. Haley, R.W., et al., *The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals.* Am J Epidemiol, 1985. **121**(2): p. 182-205.
60. Chak, K.F., C.Y. Hsiao, and T.Y. Chen, *A Study of the Effect of Shiunko, a Traditional Chinese Herbal Medicine, on Fibroblasts and Its Implication on Wound Healing Processes.* Adv Wound Care (New Rochelle), 2013. **2**(8): p. 448-455.
61. Yang, X., et al., *Protective effects of panax notoginseng saponins on cardiovascular diseases: a comprehensive overview of experimental studies.* Evid Based Complement Alternat Med, 2014. **2014**: p. 204840.
62. Ng, T.B., *Pharmacological activity of sanchi ginseng (Panax notoginseng).* J Pharm Pharmacol, 2006. **58**(8): p. 1007-19.
63. Jiao, Y., et al., *Guidelines on common cold for traditional Chinese medicine based on pattern differentiation.* J

Tradit Chin Med, 2013. **33**(4): p. 417-22.
64. Mayhall, C.G., *Hospital Epidemiology and Infection Control, Fourth Edition.* Wolters Kluwer Health, 2012(Chapter 21): p. 286.
65. Mayhall, C.G., *Hospital Epidemiology and Infection Control, Fourth Edition.* Lippincott Williams & Wilkins, a Wolters Kluwer business, 2012. **Available on: http://solution.lww.com/hospepideminfectioncontrol#tab_about**.
66. Liu, H., et al., *Sample size calculations for prevalent cohort designs.* Stat Methods Med Res, 2014.
67. Mangram, A.J., et al., *Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee.* Am J Infect Control, 1999. **27**(2): p. 97-132; quiz 133-4; discussion 96.
68. Giacometti, A., et al., *Epidemiology and microbiology of surgical wound infections.* J Clin Microbiol, 2000. **38**(2): p. 918-22.
69. Huotari, K. and O. Lyytikainen, *Impact of postdischarge surveillance on the rate of surgical site infection after orthopedic surgery.* Infect Control Hosp Epidemiol, 2006. **27**(12): p. 1324-9.
70. Sykes, P.K., et al., *When continuous surgical site infection surveillance is interrupted: the Royal Hobart Hospital experience.* Am J Infect Control, 2005. **33**(7): p. 422-7.
71. Mangram, A.J., et al., *Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee.* Infect Control Hosp Epidemiol, 1999. **20**(4): p. 250-78; quiz 279-80.
72. Schimmel, J.J., et al., *Risk factors for deep surgical site infections after spinal fusion.* Eur Spine J, 2010. **19**(10): p. 1711-9.
73. Rao, S.B., et al., *Risk factors for surgical site infections following spinal fusion procedures: a case-control study.* Clin Infect Dis, 2011. **53**(7): p. 686-92.
74. Seki, T., et al., *[Evaluation of deep infection of the surgical site after spine surgery].* No Shinkei Geka, 2013. **41**(7): p. 593-9.
75. Minnema, B., et al., *Risk factors for surgical-site infection following primary total knee arthroplasty.* Infect Control Hosp Epidemiol, 2004. **25**(6): p. 477-80.
76. Sankar, B., P. Ray, and J. Rai, *Suction drain tip culture in orthopaedic surgery: a prospective study of 214 clean operations.* Int Orthop, 2004. **28**(5): p. 311-4.
77. Ho, C., D.J. Sucato, and B.S. Richards, *Risk factors for the development of delayed infections following posterior spinal fusion and instrumentation in adolescent idiopathic scoliosis patients.* Spine (Phila Pa 1976), 2007. **32**(20): p. 2272-7.
78. Bernard, A.C., et al., *Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients.* J Am Coll Surg, 2009. **208**(5): p. 931-7, 937.e1-2; discussion 938-9.
79. *Clinical use of antibiotics hierarchical management directory in Guangdong Province China.* 2012. **Available at: http://www.gdwst.gov.cn/a/zcwj/201207279918.html**.
80. Hansen, E., et al., *Perioperative antibiotics.* J Arthroplasty, 2014. **29**(2 Suppl): p. 29-48.
81. Wang, R., et al., *Wound-healing plants from TCM: in vitro investigations on selected TCM plants and their influence on human dermal fibroblasts and keratinocytes.* Fitoterapia, 2013. **84**: p. 308-17.
82. *17 PPRC, Pharmacopoeia of the People's Republic of China. Peking, China: Chemical Industry Press7117069821; 2005.*
83. *Special Rectification Program for the Clinical Application of Antibiotics in 2013.* Available at http://www.moh.gov.cn/mohyzs/s3585/201305/6042979f05cf49609e96410d7314ecae.shtml, 2013.
84. Kurz, A., D.I. Sessler, and R. Lenhardt, *Perioperative normothermia to reduce the incidence of surgical-wound*

infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med, 1996. **334**(19): p. 1209-15.

85. Qadan, M., et al., *Perioperative supplemental oxygen therapy and surgical site infection: a meta-analysis of randomized controlled trials.* Arch Surg, 2009. **144**(4): p. 359-66; discussion 366-7.
86. Namba, R.S., M.C. Inacio, and E.W. Paxton, *Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees.* J Bone Joint Surg Am, 2013. **95**(9): p. 775-82.
87. Colman, M., et al., *Prolonged operative time increases infection rate in tibial plateau fractures.* Injury, 2013. **44**(2): p. 249-52.
88. Lin, S., et al., *Surgical site infection after open reduction and internal fixation of tibial plateau fractures.* Eur J Orthop Surg Traumatol, 2013.
89. Owens, W.D., J.A. Felts, and E.L. Spitznagel, Jr., *ASA physical status classifications: a study of consistency of ratings.* Anesthesiology, 1978. **49**(4): p. 239-43.
90. Yuan, K. and H.L. Chen, *Obesity and surgical site infections risk in orthopedics: a meta-analysis.* Int J Surg, 2013. **11**(5): p. 383-8.
91. Marchant, M.H., Jr., et al., *The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty.* J Bone Joint Surg Am, 2009. **91**(7): p. 1621-9.
92. Masgala, A., et al., *Risk factors affecting the incidence of infection after orthopaedic surgery: the role of chemoprophylaxis.* Cent Eur J Public Health, 2012. **20**(4): p. 252-6.
93. Gradl, G., et al., *Surgical site infection in orthopaedic oncology.* J Bone Joint Surg Am, 2014. **96**(3): p. 223-30.
94. Ikeanyi, U.O., C.N. Chukwuka, and T.O. Chukwuanukwu, *Risk factors for surgical site infections following clean orthopaedic operations.* Niger J Clin Pract, 2013. **16**(4): p. 443-7.
95. Abdul-Jabbar, A., et al., *Surgical site infection in spinal surgery: description of surgical and patient-based risk factors for postoperative infection using administrative claims data.* Spine (Phila Pa 1976), 2012. **37**(15): p. 1340-5.
96. Lin, W.C., et al., *New vertebral osteoporotic compression fractures after percutaneous vertebroplasty: retrospective analysis of risk factors.* J Vasc Interv Radiol, 2008. **19**(2 Pt 1): p. 225-31.
97. Ma, X., et al., *Risk factors for new vertebral compression fractures after percutaneous vertebroplasty: qualitative evidence synthesized from a systematic review.* Spine (Phila Pa 1976), 2013. **38**(12): p. E713-22.
98. Goz, V., et al., *Vertebroplasty and kyphoplasty: national outcomes and trends in utilization from 2005 through 2010.* Spine J, 2013.
99. Gruskay, J., et al., *Is surgical case order associated with increased infection rate after spine surgery?* Spine (Phila Pa 1976), 2012. **37**(13): p. 1170-4.
100. Radcliff, K.E., et al., *Adjacent segment disease in the lumbar spine following different treatment interventions.* Spine J, 2013. **13**(10): p. 1339-49.
101. Stromqvist, F., B. Jonsson, and B. Stromqvist, *Dural lesions in decompression for lumbar spinal stenosis: incidence, risk factors and effect on outcome.* Eur Spine J, 2012. **21**(5): p. 825-8.
102. Gu, Y., et al., *Incidence and risk factors of C5 palsy following posterior cervical decompression: a systematic review.* PLoS One, 2014. **9**(8): p. e101933.
103. Ikuta, K., O. Tono, and M. Oga, *Prevalence and clinical features of intraspinal facet cysts after decompression surgery for lumbar spinal stenosis.* J Neurosurg Spine, 2009. **10**(6): p. 617-22.
104. Caroom, C., et al., *Intrawound vancomycin powder reduces surgical site infections in posterior cervical fusion.* Spine (Phila Pa 1976), 2013. **38**(14): p. 1183-7.
105. Yagi, M., et al., *Incidence and the risk factors of spinal deformity in adult patient after spinal cord injury: a single center cohort study.* Eur Spine J, 2015. **24**(1): p. 203-8.

106. Sato, S., et al., *Reoperation rate and risk factors of elective spinal surgery for degenerative spondylolisthesis: minimum 5-year follow-up.* Spine J, 2015.
107. Veeravagu, A., et al., *Risk factors for postoperative spinal wound infections after spinal decompression and fusion surgeries.* Spine (Phila Pa 1976), 2009. **34**(17): p. 1869-72.
108. Durkin, M.J., et al., *Postoperative infection in spine surgery: does the month matter?* J Neurosurg Spine, 2015: p. 1-7.
109. Radcliff, K.E., et al., *What is new in the diagnosis and prevention of spine surgical site infections.* Spine J, 2015. **15**(2): p. 336-47.
110. Rodriguez-Caravaca, G., et al., *Compliance with antibiotic prophylaxis in spinal fusion surgery and surgical wound infection.* Rev Invest Clin, 2014. **66**(6): p. 484-9.
111. Linam, W.M., et al., *Risk factors associated with surgical site infection after pediatric posterior spinal fusion procedure.* Infect Control Hosp Epidemiol, 2009. **30**(2): p. 109-16.
112. Croft, L.D., et al., *Risk factors for surgical site infections after pediatric spine operations.* Spine (Phila Pa 1976), 2015. **40**(2): p. E112-9.
113. Lim, S., et al., *Risk Factors for Postoperative Infections Following Single Level Lumbar Fusion Surgery.* Spine (Phila Pa 1976), 2014.
114. Ji, X.Y., B.K. Tan, and Y.Z. Zhu, *Salvia miltiorrhiza and ischemic diseases.* Acta Pharmacol Sin, 2000. **21**(12): p. 1089-94.
115. Fourtner, C.R. and R.A. Pax, *The contractile blood vessels of the earthworm, Lumbricus terrestris.* Comp Biochem Physiol A Comp Physiol, 1972. **42**(3): p. 627-38.

15 Manuscript for submission to the Journal of Hospital Infection

Surgical Site Infection after Orthopedic Surgery Performed in Dong Guan Hospital of Traditional Chinese Medicine: A Descriptive Study of the Burden of Surgical Site Infection and its Risk factors with A Focus on Antimicrobial Prophylaxis and Traditional Chinese Medicine in Spinal Surgery

Jiancong Wang[1,3,*] Xiaoyan Lu[3] Zhiwen Zheng[3]

Gunnar Aksel Bjune[1] Hanne Merete Eriksen[2]

[1]*Department of Community Medicine, Institute of Health and Society, the Faculty of Medicine, University of Oslo, Oslo, Norway*

[2] *Department of Infectious Disease Epidemiology, Norwegian Institute of Public Health, Oslo, Norway*

[3] *Dong Guan Hospital of Traditional Chinese Medicine, affiliated to Guangzhou University of Chinese Medicine, Dong Guan City, Guang Dong Province, China*

**Corresponding author Address: Kirkeveien 166 Fredrik Holsts hus 0450 Oslo, Norway. Tel.:+47-406-18-599*

No.22 Song Shan Hu Da Dao, 523000, Dong Guan, China. Tel.:+86-137-5136-2816

E-mail address: jiancong.wang@studmed.uio.no

Jiancong.wang@outlook.com

Keywords

Surgical-site infection · Spinal surgery · Incidence rate · Risk factor · Prospective cohort study · Antimicrobials prophylaxis · Traditional Chinese Medicine

Abstract

Background: Surgical site infection (SSI) is a serious complication after orthopedic surgery, and it is associated with high morbidity rates, high healthcare costs and in some cases poor patients' outcomes. **Aims:** The purpose of this study was to identify the burden of SSI among orthopedic surgery and its associated risk factors of SSI among the people underwent spinal surgery in a selected hospital in China. **Methods:** From June 26 to November 30 in 2014, we performed a prospective surveillance study in the patients who underwent orthopedic surgery in a selected Chinese hospital. SSI was diagnosed based on the definition established by the Centers for Disease Control and Prevention (CDC) and was identified by bedside surveillance and post-discharge checkup. Detailed pre-, intra-, post-operative patient characteristics were prospectively recorded using a standardized data collection format. **Results:** A total of 287 orthopedic surgery cases, among them 192 cases of spinal surgery, were included, of which 8 cases developed surgical site infection. In the present study, wound contamination class, wound drains and blood transfusion were a surgery-related risk factor during the hospital stay after bivariate analysis. Intravenous antimicrobial prophylaxis (AMP) was given in 176 of 287 (61.3%) after orthopedic surgery. The average duration of AMP deliveries was 2.2 days (range 1-9 days). However, traditional Chinese medicine in the present study cannot conclude

on its effect to prevent SSI. **Conclusion:** In conclusion, we identified an incidence proportion of SSI after orthopedic surgery of 2.8%. The orthopedic SSI risk factors identified in present study may use to be reducing the incidence of SSI in the future.

Introduction

Surgical site infection (SSI) is a serious complication after orthopedic surgery, and it is associated with high morbidity rates, high healthcare costs and in some cases poor patients' outcomes[1]. SSIs are reported to be the third most common Healthcare Associated Infection in Europe, U.S. and China [2-5]

The magnitude of the burden of orthopedic SSI varies between different studies and different parts of the world. The incidence of surgical site infection (SSI) among patients who underwent spinal surgery ranged from 1.3% to 13.7% [3, 6-9]. Through reviewing data in China National Knowledge Infrastructure, it was identified that the incidence of SSI among patients with spinal surgery ranged from 1.8% to 7.7% across the country [10-12]. According the Guideline of Hospital Management and Assessment [13] published by Ministry of Health in China, the goal is that the overall incidence rate of SSI in clean wound surgeries should be $\leqslant$1.5%.

The incidence of SSI after spinal surgery could be influenced by patients' characteristics and pre-, intra- and post-operative factors. Following factors are shown to increase the risk of developing a spinal SSI: American Society of Anesthesiologists (ASA) score $\geq$3, inappropriate timing of prophylactic antibiotic therapy, duration of surgical procedure$\geq$ 3h, wound classified as contaminated or dirty, and length of stays [2, 14-16]. However, a systematic review [14] indicated that there is a paucity of solid evidence of robust risk factors associated with spinal surgery.

The prophylactic antibiotics administered properly can significantly reduce the incidence of SSI [17]. The American Society of Health-System Pharmacists Therapeutic Guidelines[18] shows that AMP is recommended for orthopedic spinal procedures with and without instrumentation. However, Chinese National Guideline [19] shows that AMP is not recommended in general. There is no clear recommendation that AMP should be used for orthopedic spinal procedures in China [20].

According to the clinical condition of the patients, surgeons with traditional Chinese medicine background choose selected herbs as supplementary treatment to enhance the efficacy of western medicine, with inhibiting effect on the inflammatory responses, promoting blood circulation, and reducing the swelling [21-23].

A surveillance system is a method for understanding the incidence and distribution of SSI [24]. In China, public reports of SSI, obtained via ongoing national surveillance activities, have been rare over the past decades [25]. Therefore, the main objective of the present study was to identify the burden of SSI in orthopedic surgery and its associated risk factors among people undergoing spinal surgery in a selected Chinese hospital between June 26 and November 30 in 2014.

Materials and methods

Study design and selection criteria

This is a prospective cohort study conducted in the Dong Guan Hospital of Traditional Chinese Medicine. The hospital was established in 1965, with the integrated function of medical treatment, teaching and research. It has 955 hospital-beds.

The study included all patients who underwent orthopedic surgery in the Dong Guan Hospital of Traditional Chinese Medicine between June 26 and November 30 in 2014. Surgical sites were observed 30 days after surgery for the development of SSI. Other healthcare associated infections were not recorded.

This study included all variables which were already in the hospital surveillance system, such as age, gender, ASA scores, wound contamination class, duration of surgical procedures, type and duration of AMP administration; as well as risk factors referred by CDC and identified by studied articles [10, 26-30].

Identification of SSI

All SSI-cases are defined according to the CDC-criteria [31], and SSIs are classified as superficial incisional, deep incisional or organ/space [31]. The investigator performed bed-side observation and inspected the patients' wound three days a week (Monday, Wednesday and Friday). The wounds of those patients that had prescribed antibiotics, had a temperature over 37 Degree Celsius or relevant co-morbidity that easily caused SSI were examined.

Surgeons, laboratory technicians and clinical pharmacists were asked actively to report suspected SSI-cases. The surgical sites of the patients reported were examined thoroughly.

The investigator followed up patients' post-hospital discharge by phone-interview using a pre-defined script of questionnaire for the detection of SSI. Before the phone-interview, oral informed consent was obtained. The investigator examined the incisional sites of all patients attending the out-patient clinic.

Statistical analysis

All data was electronically recorded and thereafter transferred to the department of healthcare associated infection control. The datasets were analyzed using IBM SPSS Statistics Software Version 22.0. Descriptive statistical analysis was run. Mean, 95% confidence interval (Cl), minimum and maximum of each continuous variable were calculated.

Only spinal procedures were included in risk factors analysis knowing that this was the most common procedures in this study. Patient's characteristics related to SSI were compared by using *Chi-square* test or *Fisher's exact* test for categorical variables and the by using *Wilcoxon* test for continuous variables. Associations between SSI and possible risk factors were analyzed by calculating crude Odd's Ratio (OR) using bivariate logistic regression analysis.

Results

General description and demographical characteristics

All 287 patients that had orthopedic surgeries between 26 June and 30 November in 2014 were included in the study. There were 165 females (57.5%) and 122 males (42.5%). The mean age was 54.2 years (range, 9-89 years), and it was higher among women than men (60.7 years VS 45.4 years). More demographical characteristics are found in Table I.

The most common procedures performed in this orthopedic ward were spinal surgery with 192 cases (66.9%), followed by clavicular surgery (5.2%), tibia surgery (5.2%), and anklebone surgery (4.2%). According to categorization of ICD-9-CM codes, the three most common spinal surgery procedures in the present study were vertebroplasty (51.0%), spinal decompression (14.6%), and spinal fusions (7.3%).

Among the 287 orthopedic surgeries, 8 (2.8%) patients developed SSI. All SSIs were detected among in-hospital patients. According to the CDC definition, 4 (1.4%) of infections were superficial incisional SSI, 4 (1.4%) of infections were deep Incisional SSI and no case was diagnosed with organ/space SSI. In addition, among the 192 orthopedic spinal surgeries, 7 (3.6%) patients developed SSI after spinal surgery, with 3 (1.6%) patients of superficial incisional SSI and 4 (2.1%) patients of deep incisional SSI.

Routines of antimicrobial prophylaxis and traditional Chinese medicine

Intravenous AMP was given in 176 of the 287 (61.3%) after orthopedic surgery. In addition, 34 other cases received antimicrobials treatment at the time of surgery. 174 of 176 (98.9%) received AMP within 2 hours before the orthopedic procedures. The average duration of AMP deliveries was 2.2 days (range 1-9 days). The four most common AMP prescribed were cefotiam (35.8%), cefathiamidine (22.2%), cefuroxime (17.6%) and cefamandole (9.1%). These four prescriptions contributed to 84.7% of the total AMP given. All the 8 patients who developed SSI did receive AMP.

TCM was prescribed to 219 of the 287 patients (76.3%). The three most common TCM constituents' deliveries in the present study were *Panax notoginseng saponins* (55.7%), *Salvia miltiorrhiza* (23.7%), and *Lumbricus rubellus* (11.9%).

Risk factors for spinal surgery

Bivariate analysis indicated several significant risk factors for spinal surgery, including wound contamination class (OR, 45.5; 95%Cl, 6.9-298.8), wound drains (OR, 8.8; 95%Cl, 1.0-74.6), blood transfusion (OR, 5.6; 95%Cl, 1.2-26.5) (Table II).

Discussions

Incidence proportion of SSI

This study has identified that an incidence proportion of SSI after orthopedic surgery was 2.8% (8/287), from which 3.6% (7/192) developed SSI after spinal surgery in an orthopedic ward of Dong Guan Hospital of Traditional Chinese Medicine.

The incidence of orthopedic SSI identified in this study was comparable to the statistical figures from Chinese national survey [32], but was slightly higher than the figures from ECDC report [4]. We also found that the incidence of spinal orthopedic SSI was slightly

higher compared with other types of orthopedic SSI. This finding is consistent with what's reported in the literatures [2, 4].

We suspect that the incidence proportion of SSI identified by this study might be underestimated due to no SSI being detected by post-discharge surveillance (PDS). Other studies showed that 1.7%-3.3% of SSIs were detected by PDS [31, 33-36].

A possible explanation for no SSIs being detected during post-discharge was a low attendance at the out-patients clinic for examination of incisional sites. Some patients are living far away from the Dong Guan Hospital of Traditional Chinese Medicine. They might have attended to a hospital nearby them for checkup or readmission. There was no system that synchronized information enables us to identify SSI among patients in other hospital.

In our study, 72.5% cases completed the phone-interview during post-discharge. The mean age was higher among patients not-interviewed by phone than those being interviewed (59.1 years VS 52.3 years). It is known that elder people had a risk of SSI [14]. It might be that they were SSIs among those not being interviewed.

Risk factors for spinal surgery

Wound contamination class, wound drains, and intraoperative blood transfusion were associated with the occurrence of spinal orthopedic SSI in the bivariate analysis. These risk factors are also reported by others [2, 14-16, 37, 38]. Others have identified ASA scores, instrumentation, duration of surgical procedure$\geqslant$3h, longer duration of AMP deliveries to be association with SSI after spinal surgery. However, in our study, these factors were not associated with SSI. A possible explanation is that the present study was underpowered and therefore unable to identify association between SSI and some variables.

In this study, wound contamination class as a risk factor has association with the occurrence of orthopedic spinal SSI. This finding was consistent with previous studied article [39]. Wound drains were risk factor for orthopedic spinal SSI. This result is consistent with published studies [38, 40]. The longer the drains remained in place, the higher the risk of postoperative wound infection. Drains may increase the risk of infection by causing local tissue inflammation and/or providing direct access to the surgical site for bacteria by ascending the drain tract [38, 41, 42]. Blood transfusion as a risk factors has association with

infection after orthopedic spinal surgery, which is consistent with the article published by Ho et al [43]. Blood transfusion recipients are more susceptible to surgical site infection, and blood transfusion both enhances inflammation and suppresses immunity [44].

Antimicrobials prophylaxis

In the present study, we identified that 61.3% (176/287) of the in-hospital patients were given AMP after orthopedic surgery, from which 62.5% (120/192) of the in-hospital patients were given AMP after orthopedic spinal surgery. To our knowledge, AMP is recommended for orthopedic spinal procedures with and without instrumentation[18]. However, Chinese national guideline [19, 20] shows that AMP is not recommended in general, in which there is no detailed and specific recommendation that AMP should be used for orthopedic spinal procedures in China[20]. The only exception to the guideline[19] is that the cases with high risk factors (such as total hip arthroplasty, total knee arthroplasty, instrumentation and other factors among the orthopedic surgeries) are recommended to use AMP.

In addition, we identified a first or second generation cephalosporin of AMP prescription was administered for routine of surgical prophylaxis. This finding was consistent with the recommendations [45, 46] referred by Ministry of Health in China and identified by studied article[47]. However, the mean duration of prophylactic antimicrobials administration was 2.2 days, which exceeded the recommendation to being within 24 hours postoperative period [45, 47].

Traditional Chinese Medicine

We described the use of TCM, but cannot conclude on its effect to prevent SSI, though the literatures [48, 49] have shown that TCM such as "*Panax notoginseng saponins*" prescribed in this study could induce the biological effects [22] to combat pathogens. To date, there is no scientific evidence that patient being treated with TCM is less likely to develop SSI. However, to our knowledge, this is the first study evaluating the association between the use of TCM and SSI following spinal surgery using a prospective cohort study, and thereafter more relevant researches in this area are needed.

A limitation is that the present study was underpowered and this might be an explanation to this study being unable to identify association between SSI and some variables. The result cannot be generalized due to enrolling the cases from only one orthopedic ward. This

incidence rate of SSI is therefore not a representative to the entire hospital. In PDS, the interviewers were in shortage of techniques and skills to probe the patients to respond to the PDS-questionnaire. However, the strengths of this study is that this project made available information about the burden of SSI and its risk factors in a selected hospital in China using standardized orthopedic surveillance. This study also documented the use of TCM, from which was not currently documented in published study. Finally, this study had used routine data of the surveillance system in the Dong Guan Hospital of Traditional Chinese Medicine and thus established methods for routine evaluations of the work on infection control in the hospital.

Ethical considerations

Ethical clearance was obtained both from Regionale Komiteer for Medisinsk og Helsefaglig Forskningsetikk from Norway and Ethics Committee from the Dong Guan Hospital of Traditional Chinese Medicine.

Recommendation

More studies with appropriated sample size are needed to identify risk factors associated with SSI among people undergoing spinal surgery.

PDS in this hospital should be modified. Nurses should conduct post-discharge guidance that patients report actively their medical situation of surgical incision if redness, swelling, pain and even purulent occurred. The interviewers in PDS should be trained about how to probe the patients to respond to the PDS-questionnaire.

To the risk factors identified in the present study, nursing care and attention is recommended to be paid particular to patients with wound classified as contaminated or dirty [31]; early drain removal is recommended [42]; taking close observations during and after administration of a blood transfusion is also recommended[44].

According to the international guideline, we suggest that in this orthopedic ward AMP is recommended for orthopedic spinal procedures with and without instrumentation[18]. The duration of prophylactic antimicrobials administration should be less than 24 hours [45, 47]. Bacteria isolation is recommended before antibiotics administration [50]. Narrow spectrum, less expensive antibiotics should be the first medicines choice[20].

Conclusion

In conclusion, this study has identified that an incidence proportion of SSI after orthopedic surgery was 2.8%, from which 3.6% developed SSI after spinal surgery in an orthopedic ward of Dong Guan Hospital of Traditional Chinese Medicine. Bivariate analysis indicated several significant risk factors, including wound contamination class, wound drains, blood transfusion. Intravenous AMP was given in 176 of 287 (61.3%) after orthopedic surgery. The average duration of AMP deliveries was 2.2 days (range 1-9 days). Finally, the orthopedic SSI risk factors identified in present study may use to be for reducing the incidence of SSI in the future.

Reference

[1] Ogihara S, Yamazaki T, Maruyama T *et al.* Prospective multicenter surveillance and risk factor analysis of deep surgical site infection after posterior thoracic and/or lumbar spinal surgery in adults. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association* 2015; **20**: 71-7.

[2] Xing D, Ma JX, Ma XL *et al.* A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2013; **22**: 605-15.

[3] Surveillance of surgical site infections in Europe, 2011 Based on surveillance data of 2008 and 2009. *European Centre for Disease Prevention and Control* 2011; **Available at: http://www.ecdc.europa.eu/en/publications/Publications/120215_SUR_SSI_2008-2009.pdf**.

[4] Zarb P, Coignard B, Griskeviciene J *et al.* The European Centre for Disease Prevention and Control (ECDC) pilot point prevalence survey of healthcare-associated infections and antimicrobial use. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin* 2012; **17**.

[5] WU An-hua RN, WEN Xi-mao, YI Xia-yun, HUANG Xun, XU Xiu-hua One-day prevalence survey of nosocomial infection in 159 hospitals. *Chinese Journal of Infection Control* 2005: 12-7.

[6] Caputo AM, Dobbertien RP, Ferranti JM, Brown CR, Michael KW, Richardson WJ Risk factors for infection after orthopaedic spine surgery at a high-volume institution. *Journal of surgical orthopaedic advances* 2013; **22**: 295-8.

[7] Kakimaru H, Kono M, Matsusaki M, Iwata A, Uchio Y Postoperative antimicrobial prophylaxis following spinal decompression surgery: is it necessary? *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association* 2010; **15**: 305-9.

[8] Omeis IA, Dhir M, Sciubba DM *et al.* Postoperative surgical site infections in patients undergoing spinal tumor surgery: incidence and risk factors. *Spine* 2011; **36**: 1410-9.

[9] Viqueira AQ, Caravaca GR, Rubio JA, Frances VS Surgical Site Infection Rates and Risk Factors in Orthopedic Pediatric Patients in Madrid, Spain. *The Pediatric infectious disease journal* 2013; doi 10.1097/INF.0000000000000232.

[10] Nie H, Jiang D, Ou Y *et al.* Procalcitonin as an early predictor of postoperative infectious complications in patients with acute traumatic spinal cord injury. *Spinal cord* 2011; **49**: 715-20.

[11] XU Hai-li NL-d, YE Qian-qian, XU Hua-zi, LI Xiao-cong Related factors for postoperative incisional infections in patients undergoing spinal surgery. *Chinese Journal of Nosocomiology* 2015.

[12] LIN Qing-song ZZ-m, CHEN Jian-ting Risk factors for surgical site infections after spine surgery. *The Journal of Practical Medicine,* 2014.
[13] Hospital Management Assessment Guideline (Version 2008). 2008; **Available at: http://www.moh.gov.cn/mohyzs/s3585/200806/36242.shtml**.
[14] Pull ter Gunne AF, Hosman AJ, Cohen DB *et al.* A methodological systematic review on surgical site infections following spinal surgery: part 1: risk factors. *Spine* 2012; **37**: 2017-33.
[15] Radcliff KE, Rasouli MR, Neusner A *et al.* Preoperative delay of more than 1 hour increases the risk of surgical site infection. *Spine* 2013; **38**: 1318-23.
[16] Pull ter Gunne AF, Cohen DB Incidence, prevalence, and analysis of risk factors for surgical site infection following adult spinal surgery. *Spine* 2009; **34**: 1422-8.
[17] Yang Z, Zhao P, Wang J *et al.* DRUGS system enhancing adherence of Chinese surgeons to antibiotic use guidelines during perioperative period. *PloS one* 2014; **9**: e102226.
[18] Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery. *ASHP Therapeutic Guidelines* 2013; **Available at: http://www.ashp.org/surgical-guidelines**.
[19] National Health & Family Planning Commission, P.R.China. Principle guideline for antimicrobials clinical use. Beijing. Available at http://www.moh.gov.cn/mohyzs/s3573/200804/18544.shtml.
[20] Sun J Systematic review of interventions on antibiotic prophylaxis in surgery in Chinese hospitals during 2000-2012. *Journal of evidence-based medicine* 2013; **6**: 126-35.
[21] Yang X, Xiong X, Wang H, Wang J Protective effects of panax notoginseng saponins on cardiovascular diseases: a comprehensive overview of experimental studies. *Evidence-based complementary and alternative medicine : eCAM* 2014; **2014**: 204840.
[22] Tan BK, Vanitha J Immunomodulatory and antimicrobial effects of some traditional chinese medicinal herbs: a review. *Current medicinal chemistry* 2004; **11**: 1423-30.
[23] Ng TB Pharmacological activity of sanchi ginseng (Panax notoginseng). *The Journal of pharmacy and pharmacology* 2006; **58**: 1007-19.
[24] Roy MC, Perl TM Basics of surgical-site infection surveillance. *Infection control and hospital epidemiology* 1997; **18**: 659-68.
[25] Fan Y, Wei Z, Wang W *et al.* The incidence and distribution of surgical site infection in mainland China: a meta-analysis of 84 prospective observational studies. *Scientific reports* 2014; **4**: 6783.
[26] Lonjon G, Dauzac C, Fourniols E, Guigui P, Bonnomet F, Bonnevialle P Early surgical site infections in adult spinal trauma: a prospective, multicentre study of infection rates and risk factors. *Orthopaedics & traumatology, surgery & research : OTSR* 2012; **98**: 788-94.
[27] Namba RS, Inacio MC, Paxton EW Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *The Journal of bone and joint surgery British volume* 2012; **94**: 1330-8.
[28] Cies JJ, Chan S, Hossain J, Brenn BR, Di Pentima MC Influence of body mass index and antibiotic dose on the risk of surgical site infections in pediatric clean orthopedic surgery. *Surgical infections* 2012; **13**: 371-6.
[29] Surveillance of surgical site infections in European hospitals – HAISSI protocol. Version 1.02. *European Centre for Disease Prevention and Control* 2012; **Available at: http://www.ecdc.europa.eu/en/publications/Publications/120215_TED_SSI_protocol.pdf**.
[30] Dubory A, Giorgi H, Walter A *et al.* Surgical-site infection in spinal injury: incidence and risk factors in a prospective cohort of 518 patients. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2014; doi 10.1007/s00586-014-3523-4.
[31] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *American journal of infection control* 1999; **27**: 97-132; quiz 3-4; discussion 96.

[32] WU An-hua WX-m, LI Chun-hui,REN Nan,GONG Ru-e,HUANG Xun,FENG Li,LIU Zhen-ru,MENG Li,GUO Yan-hong China national point prevalence survey on healthcare-associated infection and antimicrobial use in 2012. *Chinese Journal of Infection Control* 2014: 8-15.

[33] Huotari K, Lyytikainen O Impact of postdischarge surveillance on the rate of surgical site infection after orthopedic surgery. *Infection control and hospital epidemiology* 2006; **27**: 1324-9.

[34] Rosenthal R, Weber WP, Marti WR *et al.* Surveillance of surgical site infections by surgeons: biased underreporting or useful epidemiological data? *The Journal of hospital infection* 2010; **75**: 178-82.

[35] Kent P, McDonald M, Harris O, Mason T, Spelman D Post-discharge surgical wound infection surveillance in a provincial hospital: follow-up rates, validity of data and review of the literature. *ANZ journal of surgery* 2001; **71**: 583-9.

[36] Sykes PK, Brodribb RK, McLaws ML, McGregor A When continuous surgical site infection surveillance is interrupted: the Royal Hobart Hospital experience. *American journal of infection control* 2005; **33**: 422-7.

[37] Schimmel JJ, Horsting PP, de Kleuver M, Wonders G, van Limbeek J Risk factors for deep surgical site infections after spinal fusion. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2010; **19**: 1711-9.

[38] Rao SB, Vasquez G, Harrop J *et al.* Risk factors for surgical site infections following spinal fusion procedures: a case-control study. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2011; **53**: 686-92.

[39] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infection control and hospital epidemiology* 1999; **20**: 250-78; quiz 79-80.

[40] Seki T, Kimura T, Sugimura T *et al.* [Evaluation of deep infection of the surgical site after spine surgery]. *No shinkei geka Neurological surgery* 2013; **41**: 593-9.

[41] Minnema B, Vearncombe M, Augustin A, Gollish J, Simor AE Risk factors for surgical-site infection following primary total knee arthroplasty. *Infection control and hospital epidemiology* 2004; **25**: 477-80.

[42] Sankar B, Ray P, Rai J Suction drain tip culture in orthopaedic surgery: a prospective study of 214 clean operations. *International orthopaedics* 2004; **28**: 311-4.

[43] Ho C, Sucato DJ, Richards BS Risk factors for the development of delayed infections following posterior spinal fusion and instrumentation in adolescent idiopathic scoliosis patients. *Spine* 2007; **32**: 2272-7.

[44] Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *Journal of the American College of Surgeons* 2009; **208**: 931-7, 7.e1-2; discussion 8-9.

[45] National Health & Family Planning Commission PRC Principle guideline for antimicrobials clinical use. *Available at: http://wwwmohgovcn/mohyzs/s3573/200804/18544shtml*.

[46] Clinical use of antibiotics hierarchical management directory in Guangdong Province China. 2012; **Available at: http://www.gdwst.gov.cn/a/zcwj/201207279918.html**.

[47] Hansen E, Belden K, Silibovsky R *et al.* Perioperative antibiotics. *The Journal of arthroplasty* 2014; **29**: 29-48.

[48] Wang R, Lechtenberg M, Sendker J, Petereit F, Deters A, Hensel A Wound-healing plants from TCM: in vitro investigations on selected TCM plants and their influence on human dermal fibroblasts and keratinocytes. *Fitoterapia* 2013; **84**: 308-17.

[49] 17 PPRC, Pharmacopoeia of the People's Republic of China. Peking, China: Chemical Industry Press7117069821; 2005.

[50] Special Rectification Program for the Clinical Application of Antibiotics in 2013. *Available at* http://wwwmohgovcn/mohyzs/s3585/201305/6042979f05cf49609e96410d7314ecaeshtml 2013.

Table I General description and demographical information for patients undergoing orthopedic surgery at Dong Guan Hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014

Patient's characteristics	All orthopedic surgery
The total number of procedures (cases)	287
Male (%)	122 (42.5%)
Female (%)	165 (57.5%)
Mean age in years (range)	54.2 (9-89)
Mean days of pre-operative stay (range)	6.6 (1-33)
Mean total days of hospital stay (range)	16.8 (4-77)
Mean duration of surgery in minutes (range)	116.3 (20-575)
The number of SSI [a] (%)	8 (2.8%) [b]
The number of Superficial SSI [a] (%)	4 (1.4%) [c]
The number of Deep SSI [a] (%)	4 (1.4%) [d]
The number of SSI [a] diagnosed in-hospital (%)	8 (2.8%)

[a] *SSI: Surgical Site Infection*
[b] *7 of them were after orthopedic spinal surgery*
[c] *3 of them were after orthopedic spinal surgery*
[d] *All of them were after orthopedic spinal surgery*

Table II Risk factors of SSI among patients undergoing spinal surgery at Dong Guan hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014(N=192)

Patients characteristics (Variables)		Total number patients of operations (SSI case)	Odds ratio(95%CI) Bivariate analysis
Age	Age≤62yrs	105 (5)	Reference Cat.
	Age>62yrs	87 (2)	0.5 (0.1-2.5)
Gender	Female	130 (5)	Reference Cat.
	Male	62 (2)	0.8 (0.2-4.4)
Body Mass Index (BMI)	BMI≤25	119 (6)	Reference Cat.
	BMI>25	15 (1)	1.3 (0.2-12.0)
	Missing	58 (0)	-
Hypertension	Yes	58 (0)	-
	No	134 (7)	Reference Cat.
Diabetes mellitus	Yes	18 (0)	-
	No	174 (7)	Reference Cat.

Rheumatoid arthritis	Yes	7 (1)	5.0 (0.5-48.0)
	No	185 (6)	Reference Cat.
Bone oncology	Yes	7 (0)	-
	No	185 (7)	Reference Cat.
Pre-operative stay	≤7 Days	140 (5)	Reference Cat.
	>7 Days	52 (2)	1.1 (0.2-5.7)
Orthopedic implant	Yes	60 (4)	3.1 (0.7-14.2)
	No	132 (3)	Reference Cat.
American Society of Anesthesiologists (ASA) scores	1+2	165 (5)	Reference Cat.
	3	27 (2)	2.6 (0.5-13.9)
Wound contamination class	Class 1+2	186 (4)	Reference Cat.
	Class 3+4	6 (3)	45.5 (6.9-298.8)
Skin preparation	Yes	167 (6)	Reference Cat.
	No	25 (1)	1.1 (0.1-9.7)
The duration of operation	<3h	146 (5)	Reference Cat.
	≥3h	46 (2)	1.3 (0.2-6.8)
The number of participants in the orthopedic surgery	3-5 participants	122 (2)	Reference Cat.
	6-9 participants	70 (5)	4.6 (0.9-24.5)
Intraoperative blood loss	<500ml	162 (4)	Reference Cat.
	>500ml	30 (3)	4.4 (0.9-20.7)
Drains	Yes	81 (6)	8.8 (1.0-74.6)
	No	111 (1)	Reference Cat.
Blood transfusion	Yes	25 (3)	5.6 (1.2-26.5)
	No	167 (4)	Reference Cat.
WBC* before surgery	4-11×10^9/L	158 (5)	Reference Cat.
	>11×10^9/L	34 (2)	1.9 (0.4-10.3)
WBC* after surgery	4-11×10^9/L	106 (3)	Reference Cat.
	>11×10^9/L	49 (3)	2.2 (0.4-11.5)
	Missing	37 (1)	-
AMP deliveries	Yes	120 (7)	Reference Cat.
	No	72 (0)	-
The duration of AMP deliveries	NO-AMP	72 (0)	-
	≤1day	48 (3)	Reference Cat.
	>1day	72 (4)	0.9 (0.2-4.1)
TCM deliveries	Yes	139 (4)	Reference Cat.
	No	53 (3)	2.0 (0.4-9.4)

* *WBC: White Blood Cell*

Table III Demographic characteristics of patients undergoing spinal surgery at Dong Guan hospital of Traditional Chinese Medicine in China during 26 June to 30 November in 2014(N=192)

Characteristics	SSI(N=7)	Non-SSI(N=185)	*P*-value*
Age at surgery, mean(SD), year	60.3(15.5)	61.8(14.7)	0.553
BMI, mean (SD), kg/m^2	23.6(2.8)	23.1(2.7)	0.273
Duration of operation, mean (SD),minutes	167.1(103.3)	122.5(102.8)	0.499
Total amount of drainage, mean (SD), ml	399.2(307.1)	258.5(185.1)	0.180

*(*Wilcoxon test* was used for continuous variables)

Acknowledgements

The authors are grateful to Xinlei Ma, Kexin Qi, Weijuan Li, Fengmei Guo from the department of Healthcare Associated Infections Control and Dr. Xiongfei Huang, Dr. Yongsheng Ye from the Department of Orthopedic surgery in the Dong Guan hospital of Traditional Chinese Medicine, who worked for this project. The authors also thank Prof. Magne Thoresen and Dr. Ibrahimu Mdala from University of Oslo to support on quantitative and statistical analysis on this article.

Conflict of interest The authors declare that they have no conflict of interest.

Funding None